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American Journal of Diseases of Children

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A CHEMICAL STUDY OF WOMAN'S MILK, ESPECIALLY ITS INORGANIC CONSTITUENTS *

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AND
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NEW YORK

No extended review of the literature on the chemistry of woman's milk will be attempted in this paper. The reader is referred for this to a résumé by Nothmann[1] in 1912 and another by Talbot[2] in 1914. Quite large series of analyses have been made by many observers in which only a determination of the organic constituents and the total ash of milk was aimed at. Among the most important publications are those of Leeds,[3] Meigs[4] and Adriance[5] in this country and those of Pfeiffer[6] and Schlossman[7] in Germany.

The fat and protein content of woman's milk are now pretty definitely agreed on. The methods followed by many chemists in the sugar determination, as we shall see later, are open to criticism; and even in the total ash estimation, errors have been made owing to faulty methods.

Considering how much work has been done on the chemistry of woman's milk, it is surprising that so few investigators have concerned themselves with the composition of the ash. With the exception of Harrington and Kinnicutt[8] who analyzed a single large composite sample, almost nothing has been published in this country and very little abroad on this subject. It is true that both here and abroad isolated analyses have been reported, but they have been mainly in connection with metabolism experiments and have frequently been

* From the laboratories of the Babies' Hospital and the Rockefeller Institute for Medical Research.

* Read at the meeting of the American Pediatric Society, Lakewood, N. J., May 26, 1915.

1. Nothmann: Jahrb. f. Kinderh., 1912, lxxv, 724.
2. Talbot: Am. Jour. Dis. Child., 1914, vii, 445.
3. Leeds: Reprint, Proc. Am. Assn. Adv. Sc., 1884.
4. Meigs: Milk Analysis and Infant Feeding, Phila., 1885.
5. Adriance: Arch. Pediat., 1897, xiv, 22, 85.
6. Pfeiffer: Verhandl. d. Versamml. d. Ges. f. Kinderh., Wien., 1894, p. 126.
7. Schlossmann: Arch. f. Kinderh., 1900, xxx, 288.
8. Harrington and Kinnicutt: Rotch, Pediatrics, 1906.

made when the conditions were presumably pathologic. Even the writers who have undertaken to study the normal composition of the ash in woman's milk and who have been most extensively quoted in literature have made a surprisingly small number of observations.

The earliest modern investigator was Bunge[9] who published in 1874. Though his methods were exact, practically those in use today, so that his results can be relied on, yet his figures which have been so widely quoted were derived from two examinations of the milk of the same woman, one made on the fifteenth and the other on the eighteenth day of lactation. He used large samples, but he does not state that it was the twenty-four hours' secretion. Söldner,[10] whose work is also much quoted, published but six analyses, three of these being of colostrum and none being of milk at a later period than three and a half months. In only one instance was his examination of an individual sample. Pelka's[11] observations were but two in number, both made on composite samples. The single observations by Blauberg,[12] Abderhalden,[13] Birk[14] and de Lange[15] practically complete the list to which reference is made in literature on the salts of woman's milk up to the work of Schloss[16] in 1912.

The most important recent contribution on this subject has been made by the author last mentioned. His observations are much more numerous than those of any of the other writers. They were made on ten large individual samples of milk, eight of these being the total secretion for twenty-four hours; the other two were large samples collected during several successive days. In addition, two composite samples, obtained respectively from fifteen and sixteen women, were examined.

Schloss divides lactation into three periods: (1) colostrum period; (2) transition period extending from the colostrum to the end of the fourth week; (3) mature, or as he terms it, the period of "ripe" milk. He concludes that though the absolute values, especially of total ash and ash constituents, show great differences in individuals, the ratio of the separate constituents to one another is fairly constant. He was particularly struck by the parallelism of the total nitrogen and total ash values. From his findings he concludes that, with the exception of fat, all the constituents of milk stand in a fairly definite ratio to

9. Bunge: Ztschr. f. Biol., 1874, x, 295.
10. Cammerer and Söldner: Ztschr. f. Biol., xxxix, 173; xliv, 61.
11. Pelka: Ztschr. f. Kinderh., 1911, ii, 442.
12. Blauberg: Quoted by Engel in Sommerfeld's Handbuch der Milchkunde, Wiesbaden, 1909, 800.
13. Abderhalden: Personal communication quoted by Schloss.
14. Birk: Monatschr. f. Kinderh., 1910-11, ix, 595.
15. De Lange: Ztschr. f. Biol., 1900, xl, 527.
16. Schloss: Monatschr. f. Kinderh., 1910-11, ix, 636; x, 499.

one another. The high protein and high ash of colostrum milk, established by the earlier investigators, were confirmed by his findings. After the colostrum period these values sink rapidly, but no falling off was shown in his four mature cases taken between the twenty-sixth day and four and a half months. It was only in the milk of three women examined after ten months that a marked reduction was evident. There was no evidence to prove a relationship between the daily quantity and concentration.

In only one case were there high figures with a relatively small production of milk. The great variation in previously published figures, especially of calcium, he explains by the fact that most authors have analyzed only small portions of the twenty-four hours' secretion, and in many cases the milk was from mothers of rachitic children. Schloss concludes that there are not yet enough analyses, even including those of all previous workers, to establish a definite picture of the composition of woman's milk, particularly of the ash in the different periods of lactation.

Besides the work referred to on the entire ash, a number of authors have investigated separate salts of milk. Thus, a special study of the phosphorus has been made by Schlossmann.[17] His results from the analyses of the milk of thirty-one individual women show the following averages:

Colostrum period, 2 women	.0533
Transition period, 6 women	.0463
Mature period, 21 women	.0460
Late period, 2 women	.0360

The calcium content of milk in normal and various abnormal conditions has been studied quite exhaustively by Bahrdt and Edelstein.[18] They give results obtained by eight other investigators of normal milk, but the figures are chiefly from their own observations. They give the following values for CaO in the milk of eighty individual mothers of healthy children taken at the different periods of lactation, exclusive of authors whose results we have tabulated in our own paper. They may be grouped as follows:

Colostrum period, 4 women		.0476
Transition period, 23 women		.0397
Mature period, 51 women	1- 3 months (7) .0489 3- 5 months (32) .0411 6- 8 months (6) .0385 8-10 months (6) .0392	.0416
Late period, 2 women	14 months (1) .0452 16 months (1) .0341	.0396

In these figures it will be noted there is very little variation after the colostrum period.

17. Schlossmann: Arch. f. Kinderh., 1905, xl, 1.
18. Bahrdt and Edelstein: Jahrb. f. Kinderh., 1910, lxxii, Supplement, p. 16.

The iron content of woman's milk has also been studied by Bahrdt and Edelstein.[19] They employed the method of Neumann, in which the iron is brought down by a zinc reagent, filtered off, and dissolved in HCl; potassium iodid is then added and the freed iodin titrated with sodium thiosulphate. The amounts used for single determinations varied from about 708 c.c. to 1,300 c.c. The samples were made up of portions collected through periods of from two to four days. The milk of three nurses was studied at different times; the periods of lactation in all were between the twenty-fourth day and the sixth month. They obtained a range of .00012 to .00029 per cent. with an average value for Fe_2O_3 of .00017 per cent. The individual variations were slight.[20]

These figures for iron correspond closely with those of Söldner who from examinations of two large samples of milk taken between the third and twelfth days gives values of .00021 and .00013—an average of .00017 per cent. Iron values given by several writers are considerably higher than those quoted; but many of them have been obtained from such small samples that the results of the analyses cannot be relied on.

From the great interest which has recently developed in the metabolism of the salts, it seemed to us desirable that the question of the composition of the ash in woman's milk should be studied anew and on a more extended scale than hitherto, and that further, an effort should be made to learn more of the individual variations in the different salts by the use of large individual samples.

The chief purpose of the investigation, the results of which are herewith presented, was a study of the composition of the ash in woman's milk at the different periods of lactation. Incidentally, we have made determinations of the other constituents of milk—fat, sugar and protein—and have made a study of the methods commonly employed in milk analysis.

In all, examinations have been made of thirty-two large individual samples—in most cases the entire twenty-four hours' secretion—and of six composite samples. Following the classification suggested by Schloss, these cases have been grouped as follows: In the "colostrum" period, two individual and three composite samples; in the "transition period," three individual and three composite samples; in the "mature"

19. Bahrdt and Edelstein: Ztschr. f. Kinderh., 1910-11, i, 182.

20. Edelstein and Csonka (Biochem. Ztschr., 1912, xxxviii, 14) have recently studied the iron content of cow's milk, using large samples for analysis. When milk was carefully drawn they obtained a range of values from 0.4 to 0.7 mg. per liter, with an average of 0.5. They conclude that the iron in cow's milk is only about one-third that in woman's milk. In point of fact the amount is so small as to be negligible.

period (one to nine months) seventeen individual samples. We have classed separately in a "late" period ten cases of milk from the tenth to the twentieth month. As we were endeavoring to secure normal values, only the milk of apparently healthy women with healthy children was taken.

The value of the observations it seems to us is enhanced by the fact of the large individual samples obtained for analysis. Of those who have previously studied this subject only Schloss appears to have appreciated the importance of securing for examination the twenty-four hours' secretion from a single individual. The observations we have made on the milk of the colostrum and transition periods have not quite the same importance as those of mature milk, since in a number of instances only composite samples were available for analysis.

The results of many of the published analyses of breast milk are open to criticism, since such small samples were used for study. This applies of course chiefly to the ash, but it has also some importance in the estimation of the other constituents. As already suggested, the methods employed by many authors are now known to be unreliable, while others make no mention of methods used. For comparison with our own results we have brought together the figures for ash analyses from the other investigators in this field whose methods could be relied on.

METHODS EMPLOYED

Nitrogen.—The *Total N* was determined in both liquid and dried samples by the Kjeldahl-Gunning method. The casein was precipitated by dilute acetic acid in a cold solution and the N determined in the filtrate, thus giving, first, the percentage of total protein which is casein, and secondly, the percentage of protein not precipitated by acetic acid. The latter figure necessarily includes any nonprotein nitrogenous substances which are present in the milk; there is evidence that such substances exist. In calculating the total protein as six and a quarter times the N there is therefore a slight error.

Fat.—The fat was determined in dried material by extraction with ether according to a modification of the Soxhlet method.

Sugar.—The question of the milk sugar content of the human milk does not seem yet to be definitely settled. Authors differ considerably in the range of values which they report, some, especially among the earlier investigators, giving figures below 6 per cent., while others obtain averages of above 7 per cent., and occasional figures run above 8 per cent.

Three general methods of sugar determinations have been employed: (1) Estimation by difference; (2) by the polariscope; (3) by some reduction method. In the first it has been customary to determine separately the fat, protein and ash and to regard the difference between the sum of these and the total dried weight as sugar. All the error in the analysis is thus thrown on the sugar. This method has been and still is much used, but is open to very obvious objections. Polariscope readings require considerable correction and are regarded as unreliable by several authors, including Reiss and Sommerfeld.[21] They may

21. Reiss and Sommerfeld in Sommerfeld's Handbuch der Milchkunde, 1909.

be too low because of the presence in the milk of substances which may cause rotation to the left.

Most of the figures for milk sugar reported have been obtained by some reduction method. Reduction methods may give too high figures because of the presence of other reducing substances than lactose. Schlossmann used a reduction method but obtained the value for the reduced copper by weighing instead of by titration. His range is from 5.2 to 10.9 per cent. Söldner used the same method and reports values from 5.35 to 7.52 per cent. If there is any difficulty due to the presence of reducing substances other than lactose, it is evidently not avoided by these investigators. Lust[22] gives for twenty-five women a range of 5.7 to 8.5 per cent., averaging 7.1 per cent. He also used a reduction method but made a colorimetric determination of the reduced copper. Schloss employed the titration method, but considers it inexact and does not include his results in his tables; his figures for sugar ranged from 6.38 to 7.9 per cent.

In our analyses the sugar was estimated after removal of the protein by boiling and then adding dilute acetic acid. The sugar was then determined by a titration method with Fehling's solution, in which the copper oxid is held in solution by potassium ferrocyanid. It was found that this method gave almost invariably higher results than the polariscope, but that it agreed very well with other reduction methods, including the Volhard. Both the reduction methods and the polariscope determinations are therefore also open to criticism. There cannot be said yet to have been devised a wholly satisfactory method for sugar determination in woman's milk.[23]

On the whole the indirect method of estimating the sugar by difference, although open to the most obvious objections, appeared in our work to give the most consistent results. If this method is followed, however, a definite procedure in drying must be employed. We have dried the samples to minimum weight over the water bath and then allowed them to come to constant weight in the air at room temperature. This last step was to make sure that the lactose when weighed should contain all its water of crystallization. Cammerer and Söldner showed that the dried matter at equilibrium with the air includes the water of crystallization of milk sugar, but that if milk is brought to a constant weight in vacuo at 98 C. the lactose is in an anhydrous condition. The figures given in our tables represent the lactose with its water of crystallization. The lactose in an anhydrous form weighs 5 per cent. less. Most authors do not state which form of lactose their figures indicate. In our table we have given both the figures obtained by the reduction method and also those in which the estimation is by difference.

Ash.—The greater part of the twenty-four hours' secretion was dried on a steam bath until it reached a constant weight in equilibrium with room temperature and humidity. In this dried material the total ash and the separate ash constituents were determined. The method of ashing is of considerable importance. The one employed is that described by Karl Stölte;[24] a sufficient sample

22. Lust: Monatschr. f. Kinderh., 1912, vi, 236.

23. Since the greater part of this work was completed, a new method for removing the protein from milk, preparatory to sugar determination, has been suggested by Hill of Ithaca (Jour. Biol. Chem., March, 1915). To precipitate the protein after boiling, colloidal iron is added to the specimen of milk. This method was proposed for cow's milk. In applying this to woman's milk we have found it advantageous to add a few drops of a saturated solution of magnesium sulphate. In certain samples of milk it is impossible to obtain a clear filtrate with the acetic acid precipitation. In such cases the new procedure is of much value. By means of it we have never failed to obtain a clear filtrate. The application of this method, however, would affect the result in only a very small number of the analyses given in this paper.

24. Stölte: Biochem. Ztschr., 1911, xxxv, 104.

of the dried substance, finely ground, is weighed into a platinum dish, which is set on pieces of broken pipe-clay inside a porcelain dish of a diameter 1 to 2 inches greater than that of the platinum dish. Low heat from a large-sized Teklu burner is applied to the porcelain dish until the material is well charred; then the heat is gradually increased to the greatest possible point. When most of the black has disappeared, the platinum dish is covered by a piece of platinum foil and ignition continued until ashing is completed. This method seems to be especially advantageous in connection with the determination of sodium and potassium, since it is found that pure sodium chlorid and potassium chlorid subjected to this treatment for hours lose no weight whatever. Ash obtained in this way was used for the determination of calcium, magnesium, phosphorus, sodium and potassium.

To avoid the possibility of a slight loss of chlorin during the breaking down of the organic compounds, this constituent of the milk was determined directly in the dried material. We have followed the method of removal of the protein by ferric alum and nitric acid, and titration of the chlorids in the filtrate according to Volhard. This is similar to the method chosen by Schloss after he had carefully tested it in comparison with other methods commonly used.

Calcium, magnesium, sodium, potassium and *phosphorus* were all determined by the usual methods. Calcium was precipitated as oxalate and weighed as oxid. Magnesium was precipitated as magnesium ammonium phosphate and weighed as pyrophosphate. Sodium and potassium were separated as chlorids and the potassium determined in the combined chlorids by precipitation with platinic chlorid. By the use of the Stölte method of ashing just described, the danger of volatilization of potassium and sodium chlorids, both in the initial ashing and at the stage of driving off ammonium salts, is entirely avoided. Unless this or some similar precaution is taken the values obtained for potassium and sodium are absolutely unreliable. Phosphoric acid was precipitated as ammonium phosphomolybdate; this was dissolved by ammonia and magnesium ammonium phosphate, precipitated by magnesia mixture and weighed as pyrophosphate.

The fat, sugar, protein and total ash in milk of the different periods are given in Table 1.

Colostrum.—The chief characteristic of the milk of the colostrum period is the high protein and the high total ash. The ash in one sample (No. 3) was so much lower than all the others that it must be regarded as an exceptional individual variation. Excluding this one the average ash for the period was 0.3077, the average protein 2.25 per cent. These figures correspond fairly well with those published by other observers. The specific gravity differs little from that of the milk of other periods.

Our values for sugar are somewhat higher than those reported by other investigators. The sugar figure was obtained by reduction in but a single sample; in the others it was estimated by difference. The reason for this was that our chief purpose was a study of the salts of milk, and it was sometimes impossible to do both determinations with the amount of milk which could be obtained for examination. The fat for all the samples analyzed averaged 3.15 per cent. But one of the individual samples which was taken at the very end of the colostrum period was unusually high, 4.43 per cent. An average of the remain-

TABLE 1.—Percentage Composition of Woman's Milk

A. Colostrum Period (1 to 12 Days)

No.	Age of Woman, Yrs.	Age of Child, Days	No. of Child	Sample	Amt. in c.c.	Sp. Gr.	Total Solids	Fat	Sugar by		Protein			Ash
									Reduction	Difference	Total	Casein	Albumin	
1	19-21	3-4	....	Composite, 5 women	295	.....	12.87	2.85	....	7.66	2.06	..	....	.2960
2	18-25	3-5	....	Composite, 6 women	960	1.032	12.68	3.30	6.50	7.09	1.96	.26	1.70	.3312
3	....	5-7	....	Individual	320	1.035	12.83	2.13	....	7.92	2.60	...	....	.1747
4	....	5-8	....	Individual	240	1.032	15.05	4.43	....	7.16	2.44	..	....	.2921
5	20-25	5-12	....	Composite, 4 women	210	.....	13.67	3.05	....	8.12	2.19	...	....	.3117

B. Transition Period (12 to 30 Days)

6	16-21	12-30	....	Composite, 4 women	285	.....	15.66	5.64	....	8.18	1.61	...	....	.2335
7	32	14	....	Individual	215	1.032	10.36	1.33	....	7.76	1.06	...	....	.2132
8	20	15-18	....	Composite, 2 women	490	1.032	12.74	3.89	....	7.24	1.36	...	....	.2471
9	19-32	14-28	....	Composite, 5 women	175	.....	14.18	4.01	....	7.88	1.99	...	....	.3042
10	18	21	....	Individual	175	.....	13.77	....	....	....	1.42	...	....	.2262
11	19	21	....	Individual, 24 hours	975	1.032	13.66	3.96	7.80	7.73	1.75	.45	1.30	.2204

C. Mature Period (1 to 9 Months)

		Mos.												
12	18	1	1	Individual, 48 hours	1,075	1.024	9.81	3.07	5.54	5.44	1.17	.37	.80	.1825
13	32	2	2	Individual, 24 hours	975	1.032	10.30	1.86	8.20	7.19	1.03	.40	.63	.2200
14	24	2	3	Individual, 24 hours	1,100	1.031	11.82	2.83	7.86	7.73	1.07	.41	.66	.1902
15	26	3	2	Individual, 36 hours	1,025	1.033	10.54	1.67	8.38	7.82	0.88	.04	.84	.1717
16	25	3	2	Individual, 24 hours	800	1.036	12.16	2.93	7.05	8.06	0.96	.46	.50	.2127
17	23	3	1	Individual, 24 hours	900	.....	12.05	2.87	7.78	7.73	1.23	.51	.72	.2135
18	32	3	2	Individual, 24 hours	850	.....	14.43	4.53	7.33	8.18	1.50	.64	.86	.2254
19	27	3½	2	Individual, 24 hours	950	1.031	13.11	3.89	8.38	7.72	1.26	.46	.80	.2433
20	23	3¾	1	Individual, 24 hours	880	.....	13.45	3.74	7.27	8.36	1.16	.52	.64	.1914
21	39	4	2	Individual, 24 hours	1,050	1.033	11.31	2.59	8.45	7.50	1.01	.34	.67	.2090
22	23	4	1	Individual, 24 hours	975	1.032	12.18	3.19	8.11	7.65	1.13	.36	.77	.2141
23	26	5	1	Individual, 24 hours	975	1.031	12.38	3.76	8.38	7.29	1.10	.45	.65	.2281
24	37	6	2	Individual, 48 hours	975	1.033	11.53	2.15	8.10	8.01	1.18	.36	.82	.1922
25	30	6	4	Individual, 36 hours	1,150	1.030	12.50	3.26	7.98	8.05	1.12	.53	.59	.1590
26	30	7	2	Individual, 24 hours	840	.....	14.13	5.48	7.48	7.11	1.29	.52	.77	.2462
27	22	8½	1	Individual, 48 hours	960	1.033	13.20	4.42	7.75	7.26	1.31	.53	.78	.2158
28	28	9	1	Individual, 2 days	960	1.033	11.86	3.27	7.60	7.16	1.23	.42	.81	.1974

TABLE 1.—(*Continued*)

D. LATE PERIOD (10 TO 20 MONTHS)

No.	Age of Woman, Yrs.	Age of Child, Mos.	No. of Child	Sample	Amt. in c.c.	Sp. Gr.	Total Solids	Fat	Sugar by		Protein			Ash
									Reduction	Difference	Total	Casein	Albumin	
29	31	10	4	Individual, 4 days	450	.....	12.25	3.02	7.92	8.02	1.00	.30	.70	....
30	25	10½	1	Individual, 2 days	465	1.031	12.29	3.24	7.58	8.00	0.84	...	...	.2148
31	23	11¼	1	Individual, 2 days	480	1.036	10.00	0.97	....	7.77	1.05	...	...	.2107
32	33	12	3	Individual, 3 days	350	1.031	12.16	2.43	7.65	8.36	1.15	.35	.80	.2141
33	30	12½	4	Individual, ½ day	650	1.032	12.38	3.71	7.57	7.58	0.92	.40	.52	.1728
34	26	12½	..	Individual, 1 day	690	1.028	12.77	3.87	7.01	7.66	1.03	.42	.61	.2108
35	..	14	..	Individual, 3 days	560	.....	10.63	2.00	7.14	7.31	1.14	.05	1.09	.1790
36	30	15	4	Individual, ½ day	640	1.029	15.56	6.20	7.10	8.00	1.20	.64	.56	.1675
37	..	18	..	Individual, 5 days	615	1.030	12.30	3.51	7.47	7.40	1.17	...	...	.2251
38	35	20	6	Individual, 3 days	690	1.033	11.44	2.70	7.77	7.34	1.22	.16	1.06	.1855

ing four analyses, including three composite and one individual sample, was 2.83 per cent., which is probably much nearer the usual fat content of colostrum milk. It corresponds with the results obtained by others.

Transition.—In the transition period there is noted a striking reduction both in protein and total ash; but a considerable rise in the fat. Here again the percentage of fat in one specimen (No. 7) was so low as clearly to be an exceptional individual variation. The average for the remaining one individual and three composite samples was 4.37 per cent. The average values for the other elements were sugar 7.74; protein, 1.56; ash, 0.2581 and total solids, 13.39 per cent.

While these figures are too few in number to be regarded as more than suggestive, they indicate that the secretion of woman's milk is richer in fat, in protein, in salts and in total solids in the early weeks of lactation than at a later period. It corresponds also to the needs of the infant during the period of his most rapid growth. This, as one would expect, is most striking in the case of the ash and the protein.

Mature.—The figures for mature milk are from seventeen large individual samples—usually the twenty-four hours' secretion. Though the number of cases is small, the figures have a value which does not attach to those obtained from a study of small samples. They were all from healthy women whose infants were thriving; they were all upon a mixed diet. The age and the number of the child are given in the table. As would be expected, the figures show considerable indi-

vidual variation in all the elements; this is least in the protein and greatest in the fat. The figures for sugar are given both as obtained directly by reduction and as estimated, in the more common way, by difference. Compared with the early or transition period there is noted a fall in the total solids which affects all the elements except the sugar, but is most noteworthy in the protein and the ash.

For comparison we at first divided these into two groups: the first group of nine samples of one to four months' milk; the second of eight samples of four to nine months' milk. But the differences in the individual samples and in the averages of these two periods was so slight that a separate grouping seemed unnecessary.

The individual variations in this period are most marked in the fat, the range being from 1.67 to 5.48 per cent. The smallest variation is seen in the sugar. The lowest value found was 5.54 per cent. Except for this one specimen the range was between 7.05 and 8.38 per cent. obtained by reduction, and 7.11 and 8.36 per cent. by difference. In the main, therefore, the values obtained for sugar by the two methods do not differ greatly. The range for the total protein is from 0.88 to 1.5 per cent.; the figures in all but three of the seventeen samples fall between 1 and 1.3 per cent. The relation of the casein and albumin continues fairly uniform throughout both periods. The range in the total ash is between 0.1590 and 0.2433 per cent., but the greater number of the samples fall between 0.18 and 0.22 per cent.

In the colostrum period the relation of the ash to total protein is 1:7; in the transition period it is 1:6; throughout the mature period it is about 1:5, or the same ratio as exists in cow's milk.

Late.—Greater interest attaches to a study of the ten samples of late milk—tenth to twentieth month, for so few observations on milk of this period have been published. There are two or three exceptional findings, but as a group the milks for this period show no constant or essential differences in any of their constituents from those of the mature period. The marked fall in the protein and ash noted by some observers was not regularly seen in our cases. In but two of the ten cases was the protein low, while in five of the ten cases the ash was higher than the average of the mature period.

Excluding the three very exceptional individual variations mentioned, two of fat and one in total ash, occurring in the colostrum and transition periods, the average percentage composition of the milk for each of the different periods is as shown in Table 2.

We have brought together in Table 3 the results of the analyses found in medical literature which bear on the composition of the ash of normal woman's milk. The cases have been grouped according to the division of Schloss to whose work we are much indebted. The

total number of analyses we have been able to collect is but twenty-eight, even though we include five which are either incomplete or open to some question.

The results of our own observations on the different salts which make up the ash are given in Table 4, classified according to periods.

The variations in the total ash for the different periods have already been considered. The striking fall in the ash value continues only from the colostrum through the transition period; after this little regular variation is shown by these figures. In the samples in which the total ash was exceptionally low, while there was a reduction in all the ash constituents, it was most marked in the Na_2O and K_2O.

Of all the ash constituents the percentage of CaO continues most nearly constant throughout. This is shown not only by periods but by individual samples. In only two of the entire thirty-eight samples analyzed did the value for this element differ very widely from the

TABLE 2.—PERCENTAGE COMPOSITION OF WOMAN'S MILK BY PERIODS

Period	No. of Analyses	Fat	Sugar	Protein	Casein	Albumin	Ash	Total Solids
Colostrum, (1-12 da.).....	5	2.83	7.59	2.25	....	....	.3077	13.42
Transition, (12-30 da.).....	6	4.37	7.74	1.56	....	....	.2407	13.39
Mature, (1-9 mos.).....	17	3.26	7.50	1.15	.43	.72	.2062	12.16
Late, (10-20 mos.).....	10	3.16	7.47	1.07	.32	.75	.1978	12.18

average. Both these (Nos. 15 and 17) were individual samples of three months' milk; these two represent the range of values found, viz., 0.0295 and 0.0702 per cent.

The figures for MgO show a wider variation, not only for the different periods, but in the individual samples. The fall from the highest value in the colostrum period to the lowest in the transition period is without evident explanation. The lowest value, 0.0036 per cent., was in an individual sample of transition milk (No. 10), the highest, 0.0161, was in an individual sample in the colostrum period (No. 4).

The figures for P_2O_5 like those for CaO do not show wide variations either in the different periods or in the separate samples. The values are somewhat higher in the colostrum and transition periods; but they show no regular change till the late period when the smallest average is seen. The range is from 0.0526, an individual colostrum sample (No. 3) to 0.0212, an individual sample of a six months' milk (No. 25) in which also the total ash was the lowest met with in our observations.

TABLE 3.—Distribution of the Ash—Grams Per 100 c.c. of Milk

A. COLOSTRUM PERIOD

No.	Author	Age of Woman, Yrs.	Age of Child, Days	Sample	Amt. in c.c.	Total Ash	CaO	MgO	P_2O_5	Na_2O	K_2O	Cl	Percentage Composition of the Ash					
													CaO	MgO	P_2O_5	Na_2O	K_2O	Cl
1	Söldner.....	..	5-8	Composite, 2 women	.....	.3497	.0330	.0068	.0330	.0470	.1370	.0710	9.4	1.9	9.6	13.6	39.1	20.4
2	Söldner.....	..	5-9	Composite, 6 women	.....	.2894	.0400	.0052	.0330	.0280	.1000	.0660	13.8	1.8	11.6	9.8	34.6	22.2
3	Söldner.....	..	5-9	Composite, 6 women	.....	.3382	.0420	.0077	.0280	.0470	.0870	.0920	12.6	1.4	8.4	19.9	25.9	27.1
4	De Lange*...	..	4-10	Composite, 10 women	.....	.....	.....	.....	.....	.0950	.0640	.....	....	...	....	....	....	....
	De Lange....	..	4-10	Composite, 23 women	.....	.....	.0410	.0060	.0580	.....	.....	.0680	....	...	....	....	....	....
5	Schloss.....	22	11-13	Individual.	.....	.3048	.0335	.0039	.0380	.0532	.0795	.0892	11.0	2.2	12.4	17.4	26.0	29.2
6	Birk†.....	..	.....	.....	.....	.2814	.0360	.0093	.1137	.0544	.0770	.....	12.7	3.3	40.4	19.3	27.3	....
				Averages...	.....	.3127	.0375	.0074	.0380	.0574	.0907	.0772	11.9	2.1	10.5	16.0	30.5	24.7

B. TRANSITION PERIOD

7	Söldner.....	..	7-12	Composite, (of several women)	.....	.2620	.0350	.0070	.0330	.0360	.0790	.0570	13.5	1.7	12.7	13.7	30.1	21.8
8	Söldner.....	..	22-63	Composite, (of several women)	.....	.2185	.0410	.0044	.0320	.0170	.0680	.0360	18.9	2.0	14.5	7.9	31.1	16.3
9	Schloss.....	22	14-17	Individual	760	.2331	.0400	.0069	.0393	.0338	.0678	.0425	17.1	2.9	16.8	14.4	29.0	18.2
10	Schloss.....	22	26	Individual	1,180	.1904	.0355	.0081	.0393	.0192	.0558	.0310	18.6	4.2	20.6	10.1	28.9	16.2
11	Bunge.....	..	15	Individual	.....	.2219	.0378	.0064	.0473	.0232	.0780	.0438	14.7	2.9	21.3	10.4	35.1	19.7
12	Bunge.....	..	18	Individual (same)	.....	.2187	.0343	.0065	.0469	.0257	.0703	.0445	15.6	2.9	21.4	11.8	32.1	20.3
				Averages...	.....	.2241	.0364	.0062	.0396	.0258	.0698	0.424	16.4	2.7	17.9	11.3	31.0	18.7

C. MATURE PERIOD

13	Abderhalden	..	Mos. 2-3	.....	.....	.....	.0489	.0065	.0585	.0253	.0795	.0468	19.1	2.5	22.9	9.9	31.2	18.3
14	Schloss.....	21	2⅓	Individual	2,000	.1886	.0387	.0094	.0451	.0219	.0522	.0255	20.5	4.9	22.8	11.6	27.6	13.3
15	Schloss.....	27	3	Individual	790	.2454	.0567	.0116	.0501	.0200	.0650	.0425	23.1	4.7	20.4	8.1	26.4	17.3
16	Schloss.....	19	3½	Individual	1,360	.1848	.0370	.0100	.0342	.0192	.0549	.0308	20.0	5.4	18.5	10.3	29.7	16.7
17	Schloss.....	27	4½	Individual	1,680	.2088	.0455	.0087	.0416	.0210	.0608	.0411	21.8	4.1	19.9	10.0	29.1	19.7
18	Schloss.....	..	.....	Composite	.....	.1913	.0386	.0076	.0447	.0162	.0529	.....	20.1	3.9	23.3	8.4	27.6	....
19	Schloss.....	..	.....	Composite	.....	.1838	.0380	.0073	.0383	.0196	.0536	.0312	20.7	3.9	20.8	10.6	29.1	16.9
20	Söldner.....	..	3½	Individual	.....	.1790	.0350	.0090	.0260	.0180	.0560	.0330	19.4	3.5	14.4	10.1	32.8	18.3
21	Blauberg....	..	.....	.....	.....	.1988‡	.0394	.0068	.0294	.0049	.0600	.0294	19.8	3.4	14.7	2.4	34.7	14.7
22	Pelka.....	..	.....	Composite	.....	.1828	.0474	.....	.0387	.0258	.0848	.0294	25.9	...	21.1	14.1	46.3	16.0
23	Pelka.....	..	.....	Composite	.....	.2484	.0328	.....	.0450	.0165	.0643	.0244	13.2	...	18.1	6.6	25.9	9.8
24	Backhaus and Cronheim	..	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	17.4	3.2	14.8	7.9	33.7	15.5
25	Backhaus and Cronheim	..	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	15.5	2.1	11.8	15.9	27.3	23.9
				Averages...	.....	.1955	.0416	.0082	.0409	.0189	.0632	.0340	19.5	3.7	18.5	10.3	30.7	17.5

D. LATE PERIOD

26	Schloss.....	21	11	Individual	1,650	.1476	.0285	.0073	.0349	.0177	.0440	.0028	19.3	4.9	23.6	12.3	29.8	15.4
27	Schloss.....	..	11½	Individual	720	.1508	.0305	.0073	.0376	.0156	.0449	.0255	20.2	4.8	24.9	10.4	29.8	16.9
28	Schloss.....	26	14½	Individual	1,075	.1552	.0280	.0082	.0431	.0162	.0465	.0251	28.0	3.9	27.7	10.4	29.9	16.1
				Averages...	.....	.1512	.0210	.0069	.0385	.0165	.0451	.0211	22.5	4.4	25.4	11.0	29.8	16.1

* De Lange's work is usually quoted as a single, complete analysis. The original publication shows that part of the ash was determined from one sample, and the other elements from a second.

† Birk's figures are often quoted and hence are introduced. His value for P_2O_5 differs so widely from other published figures, as well as ours, that we have omitted this case in computing the averages.

‡ By addition, the figure by determination is not given in the original paper.

TABLE 4.—DISTRIBUTION OF THE ASH—GRAMS PER 100 C.C. OF MILK

A. COLOSTRUM PERIOD

No.	Age of Woman, Yrs.	Age of Child, Days	No. of Child	Sample	Total Ash	CaO	MgO	P_2O_5	Na_2O	K_2O	Cl
1	19-21	3-4	....	Composite, 5 women	.2960	.0431	.0092	.0308	*	*	.0640
2	18-25	3-5	....	Composite, 6 women	.3312	.0527	.0053	.0369	.0453	.0938	.0744
3	.....	5-7	....	Individual	.1747	.0476	.0076	.0526	*	*	.0304
4	.....	5-8	....	Individual	.2921	.0415	.0161	.0501	*	*	.0693
5	20-25	5-12	....	Composite, 4 women	.3117	.0382	.0125	.0347	*	*	.0462

B. TRANSITION PERIOD

6	16-21	12-30	....	Composite, 4 women	.2335	.0450	.0071	.0497	*	*	.0590
7	32	14	....	Individual	.2132	.0338	.0049	.0308	*	*	.0639
8	20	15-18	....	Composite, 2 women	.2471	.0437	.0073	.0370	.0392	.0585	.0598
9	19-32	14-28	....	Composite, 5 women	.3042	.0498	.0067	.0597	*	*	.0955
10	18	21	....	Individual	.2262	.0389	.0036	.0419	.0136	.0811	.0368
11	19	21	....	Individual, 24 hours	.2204	.0343	.0051	.0433	.0239	.0731	.0334

C. MATURE PERIOD

12	18	Mos. 1	1	Individual, 48 hours	.1825	.0413	.0052	.0265	.0183	.0480	.0251
13	32	2	2	Individual, 24 hours	.2200	.0497	.0092	.0276	.0131	.0638	.0423
14	24	2	3	Individual, 24 hours	.1902	.0414	.0084	.0317	.0148	.0502	.0364
15	26	3	2	Individual, 36 hours	.1717	.0295	.0057	.0239	.0214	.0494	.0352
16	25	3	2	Individual, 24 hours	.2127	.0459	.....	.0431	*	*	.0383
17	23	3	1	Individual, 24 hours	.2135	.0702	.0089	.0409	.0145	.0366	.0378
18	32	3	2	Individual, 24 hours	.2254	.0536	.0106	.0392	.0143	.0618	.0313
19	27	3½	2	Individual, 24 hours	.2433	.0655	.0091	.0440	.0175	.0714	.0378
20	23	3¾	1	Individual, 24 hours	.1914	.0503	.0090	.0310	.0250	.0504	.0318
21	39	4	2	Individual, 24 hours	.2090	.0456	.0067	.0331	.0129	.0599	.0437
22	23	4	1	Individual, 24 hours	.2141	.0535	.0077	.0366	.0112	.0633	.0313
23	26	5	1	Individual, 24 hours	.2281	.0545	.0072	.0386	.0126	.0661	.0320
24	37	6	2	Individual, 48 hours	.1922	.0412	.0082	.0299	.0158	.0582	.0315
25	30	6	4	Individual, 36 hours	.1590	.0354	.0072	.0212	.0031	.0545	.0304
26	30	7	2	Individual, 24 hours	.2402	.0513	.0084	.0514	.0133	.0644	.0376
27	22	8½	1	Individual, 48 hours	.2158	.0430	.0092	.0380	.0169	.0688	.0444
28	38	9	1	Individual, 2 days	.1974	.0426	.0097	.0301	.0204	.0581	.0358

* The values for Na and K in the earlier samples have not been included in the table because the method of ashing the dried material, and later of igniting to drive off ammonium salts, was one in which a slight loss of Na and K by volatilization is possible. The Stolte method described elsewhere in the paper was used in the case of most of the other samples.

TABLE 4.—(*Continued*)

D. LATE PERIOD

No.	Age of Woman, Yrs.	Age of Child, Mos.	No. of Child	Sample	Total Ash	CaO	MgO	P_2O_5	Na_2O	K_2O	Cl
29	31	10	4	Individual, 4 days	.....	.....	.....	.0281	.0126	.0469	.0439
30	25	10½	1	Individual, 2 days	.2148	.0433	.0097	.0282	.0282	.0490	.0474
31	23	11¼	1	Individual, 2 days	.2107	.0483	.0045	.0348	.0133	.0594	.0405
32	33	12	3	Individual, 3 days	.2141	.0405	.0071	.0332	.0315	.0673	.0570
33	30	12½	4	Individual, ½ day	1728	.0390	.0059	.0227	.0188	0.504	.0339
34	26	12½	....	Individual, 1 day	.2108	.0320	.0072	.0297	.0338	.0551	.0521
35	..	14	....	Individual, 3 days	.1790	.0396	.0093	.0270	.0134	.0545	.0441
36	30	15	4	Individual, ½ day	.1675	.0348	.0093	.0296	.0146	.0556	.0301
37	..	18	....	Individual, 5 days	.2251	.0461	.0054	.0422	.0151	.0576	.0500
38	35	20	6	Individual, 3 days	.1855	.0280	.0048	.0284	.0135	.0794	.0433

AVERAGES FOR THE DIFFERENT PERIODS

	No. of Analyses	Total Ash	CaO	MgO	P_2O_5	Na_2O	K_2O	Cl
Colostrum (1-12 days).....	5	.3077	.0446	.0101	.0410	.0453	.0938	.0568
Transition (12-30 days).....	6	.2407	.0409	.0057	.0404	.0255	.0709	.0580
Early mature (1-4 months)..	9	.2056	.0486	.0082	.0342	.0154	.0539	.0351
Middle mature (4 9 months)	8	.2069	.0458	.0074	.0345	.0132	.0609	.0358
Late milk (10-20 months)....	10	.1978	.0390	.0070	.0304	.0195	.0575	.0442

For reasons already mentioned (see note to Table 4) we have reported only a single figure for Na_2O and K_2O in the colostrum period, and but three in the transition period. These figures indicate the highest value for Na_2O in the colostrum period, next in the transition period, while during the early and latter part of the mature period it falls to less than one-third the amount. It is noteworthy that three of the ten late milks show a very high sodium figure; the figures for the other samples correspond with those of the mature period. The extreme individual variations of sodium are considerable in the mature period—from 0.0031 (No. 25) to 0.0250 (No. 20); but in the remaining cases of this period the value for this constituent is very close to the average.

Like Na_2O the value for K_2O is highest in the colostrum period and next in the transition period, but after this time it is quite uniform even in the late period. The individual variations are smaller than in the case of the sodium.

TABLE 5.—Percentage Composition of the Ash

A. COLOSTRUM PERIOD

No.	Age of Woman, Yrs.	Age of Child, Days	No. of Child	Sample	Total Ash	CaO	MgO	P_2O_5	Na_2O	K_2O	Cl
1	19-21	3-4	....	Composite, 5 women	.2960	14.6	3.1	10.4	....	....	21.6
2	18-25	3-5	....	Composite	.3312	15.9	1.6	11.2	13.7	28.1	22.5
3	.....	5-7	....	Individual	.1747*	27.2	4.4	30.1	....	....	17.4
4	.....	5-8	....	Individual	.2921	14.2	5.5	17.2	....	....	23.7
5	20-25	5-12	....	Composite, 4 women	.3117	12.3	4.0	11.1	....	....	14.8

B. TRANSITION PERIOD

6	16-21	12-30	....	Composite, 4 women	.2335	19.3	3.0	21.3	....	....	25.3
7	32	14	....	Individual,	.2132	15.9	2.3	14.4	....	....	30.0
8	20	15-18	....	Composite, 2 women	.2471	17.7	3.0	15.0	15.9	23.5	24.2
9	19-32	14-28	....	Composite, 5 women	.3042	16.4	2.2	13.1	....	....	31.4
10	18	21	....	Individual	.2262	17.2	1.6	18.5	6.0	35.8	16.3
11	19	21	....	Individual, 24 hours	.2204	15.6	2.3	19.6	10.8	33.2	15.1

C. MATURE PERIOD

		Mos.									
12	18	1	1	Individual, 48 hours	.1825	22.6	2.8	14.5	10.0	26.3	13.8
13	32	2	2	Individual, 24 hours	.2200	22.6	4.2	12.6	6.0	29.0	19.0
14	24	2	3	Individual, 24 hours	.1902	21.8	4.4	16.7	7.8	26.4	19.2
15	26	3	2	Individual, 36 hours	.1717	17.2	3.3	13.9	12.5	28.8	20.5
16	25	3	2	Individual, 24 hours	.2127	21.6	1.3	20.2	....	31.9	18.0
17	23	3	1	Individual, 24 hours	.2135	32.9	4.2	19.2	6.8	17.1	17.7
18	32	3	2	Individual, 24 hours	.2254	23.8	4.7	17.4	6.3	27.4	13.9
19	27	3½	1	Individual, 24 hours	.2433	22.8	3.7	18.1	7.2	29.4	15.5
20	23	3¾	2	Individual, 24 hours	.1914	26.3	4.7	16.2	13.1	26.3	16.6
21	39	4	1	Individual, 24 hours	.2090	21.8	3.2	15.8	6.2	28.7	20.9
22	23	4	1	Individual, 24 hours	.2141	25.0	3.6	17.1	5.2	29.6	14.6
23	26	5	2	Individual, 24 hours	.2281	23.9	3.2	16.9	5.5	29.0	14.0
24	37	6	4	Individual, 48 hours	.1922	21.4	4.3	15.6	8.2	30.3	16.4
25	30	6	2	Individual, 36 hours	.1590	22.3	4.5	13.3	2.0	34.3	19.1
26	30	7	1	Individual, 24 hours	.2402	21.4	3.5	21.4	5.5	26.8	15.7
27	22	8½	1	Individual, 48 hours	.2158	19.9	4.3	17.6	7.8	31.8	20.6
28	28	9	....	Individual, 2 days	.1974	21.6	4.9	15.3	10.4	27.0	18.2

* This is so exceptional a figure that the values are excluded in computing the averages.

TABLE 5.—(*Continued*)

D. LATE PERIOD

No.	Age of Woman, Yrs.	Age of Child, Mos.	No. of Child	Sample	Total Ash	CaO	MgO	P_2O_5	Na_2O	K_2O	Cl
29	31	10	4	Individual, 4 days	†						
30	25	10½	1	Individual, 2 days	.2148	20.2	4.5	13.1	13.1	22.8	22.1
31	23	11¼	1	Individual, 2 days	.2107	22.9	2.1	16.5	6.3	28.2	19.2
32	33	12	3	Individual, 3 days	.2141	18.9	3.3	15.5	14.7	31.4	26.6
33	30	12½	4	Individual, ½ day	.1728	22.6	3.4	13.2	10.9	29.2	19.6
34	26	12½	....	Individual, 1 day	.2108	15.2	3.4	14.1	16.1	26.2	24.8
35	..	14	....	Individual, 3 days	.1790	22.1	5.2	15.1	7.5	30.4	24.6
36	30	15	4	Individual, ½ day	.1675	20.8	5.6	17.7	8.7	33.2	18.0
37	..	18	....	Individual, 5 days	.2251	20.4	2.4	18.8	6.7	25.6	22.2
38	35	20	6	Individual, 3 days	.1855	15.1	2.6	15.3	7.3	42.8	23.4

† Percentage could not be calculated as total ash was not determined.

AVERAGE PERCENTAGE COMPOSITION OF ASH FOR THE DIFFERENT PERIODS

	CaO	MgO	P_2O_5	Na_2O	K_2O	Cl
Colostrum	14.2	3.5	12.5	13.7	28.1	20.6
Transition	17.0	2.4	16.9	10.9	30.8	22.9
Mature	23.3	3.7	16.6	7.2	28.3	16.5
Late	19.8	3.6	15.5	10.1	28.8	22.3

The figures for Cl vary much like the two constituents just mentioned; in all periods they bear a very close relation to the combined values of Na_2O and K_2O, indicating that it is combined as chlorids of sodium and potassium in the milk. The P_2O_5 and the CaO have also a close relationship in all periods, indicating their existence in milk as calcium phosphate.

Considering the milk by periods, we note that the high ash of the colostrum period is chiefly due to the higher values for Na_2O and K_2O; the values for CaO and P_2O_5 differing but slightly from those of the later periods. The values of the transition period show a further fall in Na_2O and K_2O and Cl, but little change in the other elements.

No constant or essential differences are seen in the values for the salts which make up the ash in either the early or latter part of the mature period, nor, in fact, even in the late period. These were grouped separately for the purpose of determining whether such a difference existed. Even in the late period the values show very little difference from those in the preceding period.

Some details of the women furnishing the late milks are interesting. In four instances (Nos. 29, 33, 34 and 36) the supply was still abundant and nursing was being carried on successfully (Nos. 33 and 36 were from the same woman). Three samples (Nos 30, 35, 38) were taken at the very end of a previously successful lactation, two or three days' pumping being usually required to obtain sufficient milk for analysis. In three cases (Nos. 31, 32, 37) there was still a good supply of milk, the infants being partly nursed and partly fed.

From a practical standpoint the best idea of the salts of woman's milk is obtained from a study of the percentage composition of the ash. This is given in the Table 5.

A comparison of the percentage composition of the salts of woman's milk, mature period, with those of cow's milk is highly instructive. The figures for cow's milk are the averages of nine analyses of our own, made of milk from mixed herds.

TABLE 6.—COMPARISON OF THE PERCENTAGE COMPOSITION OF THE ASH OF WOMAN'S AND COW'S MILK

	CaO	MgO	P_2O_5	Na_2O	K_2O	Cl
Mature woman's milk	23.3	3.7	16.6	7.2	28.3	16.5
Cow's milk	23.5	2.8	26.5	7.2	24.9	13.6

The close correspondence between these figures is very striking. In all the constituents except P_2O_5 the percentages of the different salts in the two milks are practically the same. The higher proportion of phosphorus in cow's milk is due to the large amount in the casein. Though the *proportions* of the different salts of the ash in cow's milk are so nearly those of woman's milk, the *amount* in cow's milk is about three and a half times as great. Unless, therefore, cow's milk has been diluted with more than twice its volume, the amount of these inorganic constituents furnished to the infant is equal to that which he receives in woman's milk. The addition of lime or other inorganic salts to cow's milk because they are lacking in amount is therefore quite unnecessary in infant feeding.

A general comparison of the results of our analyses with those of the other authors cited shows a general agreement in most of the essential points. There is, however, less variation between the findings in our individual cases than between the findings of the different investigators who have made but a small number of analyses. It is not unlikely that differences in methods or in technic may be responsible, in part, at least, for some of these wider variations. We feel that enough analyses of the salts of normal woman's milk have now been

made to afford a basis for comparison with abnormal milks studied in connection with metabolism observations.

There remains for brief discussion a consideration of the iron content of milk. For reasons already given, we have not undertaken a study of this part of the subject. The results of the analyses of the authors quoted in the earlier part of the paper indicate that the figures previously given for iron are too high; that woman's milk contains but 1.7 mg. of iron in a liter, while cow's milk has barely one-third as much —really a negligible quantity. By these figures iron forms but 0.00007 per cent. of the ash of cow's milk, and 0.00015 per cent. of the ash of woman's milk.

SUMMARY

1. The use of large individual samples of milk for analyses has advantages not offered by such small ones as have been commonly employed. For a determination of the inorganic constituents large samples are indispensable.

2. In the colostrum period woman's milk has high protein and high ash with rather low fat; in the transition period the protein and ash are lower while the fat is higher; in the mature period (after one month) the composition of normal milk does not vary in any essential or constant way quite up to the end of lactation. The only striking feature of late milk is a decline in quantity, though there is noted a slight fall in all the solid constituents except the sugar.

3. Of the different constituents of milk the least variation both in individuals and in periods is seen in the sugar. The proportion of this is somewhat higher than the generally accepted 7 per cent.; 7.5 per cent. is nearer the correct figure.

4. The greatest individual variations are seen in the fat, though the period variations in fat are not marked.

5. The protein is highest in the colostrum period and falls to a little over half the proportion in mature milk, during which period it is seldom over 1.25 per cent.; of this about one-third is casein, and two-thirds lactalbumin.

6. The high ash of the colostrum period is chiefly due to the amount of Na_2O and K_2O. Of the salts which make up the ash, the greatest individual, as well as the greatest period, variations are seen in the Na_2O; the least individual and period variations are seen in the CaO, the proportion of which is nearly constant throughout the period of lactation.

7. The largest constituent of the ash of woman's milk is K_2O; this with the CaO together make up more than half the total ash.

8. Although in amount the total ash of cow's milk is about three and one-half times as great as that of woman's milk, the proportion of different salts which make up the ash is nearly the same, the only exceptions being that cow's milk has more P_2O_5 and less iron.

We desire to express our thanks to those who have assisted us in obtaining specimens of milk for examination; especially to Dr. Herman Schwarz, Prof. J. Clifton Edgar, Dr. F. C. Freed and to the House Staff of the New York Foundling Hospital.

STUDIES IN THE ADAPTATION OF AN ARTIFICIAL FOOD TO HUMAN MILK*

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INTRODUCTION BY H. J. GERSTENBERGER

In 1910, the physiologist, Friedenthal[1] again picked up the threads which led to the ideal set up by the pediatrist Biedert a generation ago; namely, to the production of an artificial milk similar in all its important characteristics to the best food for the human infant, namely, breast milk. By not getting the results that it had expected from mixtures which took into consideration the quantities of protein, lactose, and fat in human milk, the pediatric world became discouraged and considered the production of an artificial human milk that would give good practical results a hopeless task. Friedenthal gathered courage for another attempt for the solution of this important and interesting problem from the fact that the salt content and the physical-chemical characteristics of human milk had been entirely neglected, and also from the conviction that these were important, if not the most important individual factors to be considered in the making of an artificial food that was to be similar to breast milk and which would give satisfactory results. Müller and Schloss,[2,4] and Helbich[3] had also independently of Friedenthal begun with the attempt to come closer to the composition of breast milk. They received their stimulus from Finkelstein's theory of the injuriousness of the whey of cow's milk. Their first object, therefore, was to modify by reduction the deleterious

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* For the apparatus, the materials and help used in making G-R milk, we are indebted to the Walker-Gordon Laboratory, Cleveland, Ohio.

* Presented at the Annual Meeting of the American Pediatric Society, Lakewood, N. J., May 24, 1915.

1. Friedenthal, H.: Ueber die Eigenschaften künstlicher Milchsera und ueber die Herstellung eines künstlichen Menschenmilchersatzes, Zentralbl. f. Physiol., 1910, xxiv, 687.

2. Müller, Erich, and Schloss, Ernst: Die Versuche zur Anpassung der Kuhmilch an die Frauenmilch zu Zwecken der Säuglingsernährung, Jahrb. f. Kinderh., 1914, lxxx, 42.

3. Helbich, H.: Die Bedeutung der Molkenreduktion für die Ernährung junger Säuglinge, Jahrb. f. Kinderh., 1910, lxxi, 655.

4. Schloss, E.: Ueber Säuglingsernährung, Berlin, 1912, S. Karger.

whey of cow's milk. They, however, encouraged by the favorable results that they had had in their institution with high fat milks, also attempted to simulate more accurately than heretofore the composition of breast milk. Schloss stated in his address at the Königsberger meeting of the Gesellschaft für Kinderheilkunde in 1910, that he and his co-workers were convinced that the road that they were following would ultimately lead to the solution of the problem of the producton of an adequate artificial food. So while they had visions of accomplishments along this direction, Friedenthal[1] had already, from theoretical grounds, worked out a plan according to which a more complete adaptation of an artificial food to breast milk could be obtained. In his article Friedenthal states that artificial woman's milk ought to contain 0.7 per cent. casein, 0.8 per cent. albumin and globulin, 7 to 8 per cent. milk sugar, 3½ per cent. fat, ash, a freezing point of —0.56, degrees electrical conductivity of 23×10^{-4} at 18 degrees, neutral reaction (H Ion Content 5×10^{-8}) besides traces of nuclein, lecithin and albuminoids, and have the proper energy content. Friedenthal further states in a later contribution (note 20) that the correlation of the salt components is of greater importance than is the total ash content.

Schloss[2, 4] then tried out Friedenthal's milk but did not get satistory results and, therefore, again modified this product. Schloss, in order to have more accurate data as to the ash composition of human and cow's milk, himself made analysis. The analyses on breast milk made by Schloss are of great value because he was the first to use samples of twenty-four hour quantities of breast milk for his determinations. In addition, he took samples of a mixed milk composed of full twenty-four hour specimens of eight women. The analyses that he got differed from those accepted up to that time. His further work, therefore, was based on the more dependable, analytical figures obtained by himself in this manner. Schloss,[4] however, felt that the poor results that he had obtained with Friedenthal's milk were due mainly to the lactose content, and he therefore replaced this with the preparation containing maltose and dextrin, and oftentimes in addition cornstarch. He also added a proprietary preparation of sodium caseinate to bring up the protein content.

By making these changes Schloss really left the road that leads to the complete adaptation of an artificial food to woman's milk, and, therefore, Friedenthal's milk, although based on less accurate analytical data, comes closer to the accomplishment of this ideal than does Schloss' milk.

Bahrdt[5] reports favorably his experience with the feeding of this milk in eighty-one cases. He states that at least among the children

5. Bahrdt, H., Bamberg, Edelstein, Hornemann: Ernährungsversuche mit Friedenthalscher Milch, Ztschr. f. Kinderh., Orig., 1914, x, 303.

of the Kaiserin Augusta Victoria-Haus, Friedenthal's milk promises better results than those obtained with mixtures of simple dilutions with carbohydrate additions. Although the analytical and the metabolism work presented in his article has been seemingly justly criticized by Müller and Schloss,[2] this fact does not necessarily disprove the good clinical results obtained by Bahrdt. It was the writer's impression when he in 1913 personally conversed with Bahrdt regarding his results with Friedenthal's milk that this food did really give good results and did mean a distinct addition to our means. Both in the personal conversation and in the article which Bahrdt published later, he emphasized the nearly universal presence of vomiting and marked spitting and of dyspeptic stools in most of the infants fed with this food.

This fact, together with the interesting and important experimental data obtained by Huldschinsky,[6] namely, (1) that the stomach of infants fed with human milk contains very small amounts of the low volatile fatty acids; (2) that the stomach of infants fed with cow's milk contains three to six times as much; (3) that the amount of the low volatile fatty acids found in the stomach of babies fed with cow's milk corresponds to the amount of fat in the milk; and (4) that the formation of these free low volatile fatty acids in the stomach of a healthy infant fed on cow's milk is caused by the splitting of the glycerids of these acids by a ferment, and that the type of the former low volatile fatty acids found in the stomach corresponds to the type existing in a preformed state in the milk fat, led me to believe that probably the qualitative differences between cow's milk fat and breast milk fat were to blame, in a large measure at least, for the excessive spitting, vomiting, and dyspeptic stools.

It is a recognized fact that cow's milk fat contains many more of the low volatile fatty acids than does breast milk fat (10 per cent. to 1.6 per cent. Langstein and Meyer[7]), and there are those—Bokai,[8] Bahrdt,[9] Czerny,[10] and others—who believe that the low volatile fatty acids play an important part in the production of acute nutritional dis-

6. Huldschinsky, K.: Untersuchungen über die Pathogenese der Verdauungsstörungen im Säuglingsalter; Mitteilung, V.: Ztschr. f. Kinderh., Orig., 1912, III, 366.

7. Langstein-Meyer: Säuglingsernährung und Säuglingsstoffwechsel, Ed. 2 and 3, pp. 22, 23, 29 and 133.

8. Bokai, A.: Experimentelle Beiträge zur Kenntniss der Darmbewegungen. C. Ueber die Wirkung einiger Bestandteile der Fäces auf die Darmbewegungen, Arch. f. exper. Path. u. Pharmokol., 1888, xxiv, 153.

9. Bahrdt, H., and McLean, Stafford: Untersuchungen über die Pathogenese der Verdauungsstörungen im Säuglingsalter; VIII. Mitteilung, Ztschr. f. Kinderh., Orig., 1914, xi, 143.

10. Czerny-Keller: Des Kindes Ernährung Ernährungsstörungen und Ernährungstherapie, Abt. 7, p. 137, Franz Deuticke, Wien, 1909.

turbances in infants. While Bahrdt[11] states that Huldschinsky's findings of the abscence of an increase in the low volatile fatty acid content in the stomach of infants ill with acute nutritional disturbances speak against the importance of the low fatty acid content of infants' stomachs, on the other hand, he does believe that a disturbance of the motor and secretory powers of the stomach might alter conditions in the stomach and upper intestine in a manner that would permit the low fatty acids of the stomach contents to play an important etiologic rôle. It seemed plausible to the writer to imagine that if, for instance, the function of the pylorus could be disturbed in a manner that would permit larger quantities of food to enter the duodenum than it would under normal circumstances, that then the actual per cent. of low volatile fatty acids in the stomach contents at the time might be an important factor in the production of an acute nutritional disturbance and in the determining of the severity of the same, and that, therefore, the relatively large per cent. of low volatile fatty acids in cow's milk fat might be of decided etiologic importance. He therefore decided to attempt to obtain a fat, vegetable or animal, or a combination of such fats, that would give the same per cent. of the low volatile fatty acids as found in the fat of breast milk. In the first conference which I had, during December, 1913, with Dr. H. D. Haskins, Assistant Professor of Biological Chemistry at Western Reserve University, regarding this plan, the practical question of mixing such a fat with Friedenthal's milk was considered. It was immediately realized that the only hope lay in the use of an homogenizer, in which I had become interested a few years previously in an attempt at the Walker-Gordon Laboratory to make a very fine curd for casein milk. It was then learned that the Belle Vernon-Mapes Dairy Company was planning to put an homogenizer in the new plant which they were building, and it was therefore decided to wait with the practical work until the homogenizer had arrived, and in the meantime finish, if possible, our theoretical plans. In the literature I came across Arnold's[12] work, "*Ueber Frauenmilchfett*," in which he makes a statement that it is possible to make out of a mixture of 14 per cent. cocoanut oil and 86 per cent. lard, of the following characteristics:

	Cocoanut Oil	Lard
Refraction	35.1	47.7
Saponification number	259.0	197.5
Reichert-Meissl number	9.0	0.4
Iodin number	8.5	53.0
Polenske number	15.8	0.15

11. Bahrdt, H., Edelstein, F., Hanssen, P., Welde, E. F.: Untersuchungen ueber die Pathogenese der Verdauungsstörungen im Säuglingsalter; X. Mitteilung, Ztschr. f. Kinderh., Orig., 1914, xi, 416.

12. Arnold, W.: Ueber Frauenmilchfett, Ztsch. f. Untersuch. d. Nahrungs- u. Genussmittel, 1912, xxiii, 433.

a fat that would give a refraction, saponification number, Reichert-Meissl number, iodin number, and Polenske number, very close to that of the fat of breast milk. It was decided, therefore, to use these data in the experimental and clinical work as soon as the homogenizer had arrived. While we were waiting, Niemann's[12] article on "Ueber die Möglichkeit einer Fettanerreichung der Säuglingsnahrung," appeared. He evidently had in mind the same goal as I, but had decided to reach it over another route, namely, over that of washed butter. Inasmuch as he claimed in his article to get an adequate removal of the low fatty acids from the butter by washing it with water, and also by vigorous stirring of a heated mixture an adequate and permanent emulsion of fat, together with Drs. Haskins and Ruh, I set myself at work to carry out Niemann's suggestion regarding the freeing of butter from the low volatile fatty acids with the idea of adding this fat to Friedenthal's milk. We hoped that by heating and vigorous stirring we were to accomplish the same permanent emulsification that Niemann[13] had obtained, with what results will be stated later.

The work of Funk[14] regarding vitamines, and his theory on the etiology of rickets, the work of Osborne and Mendel,[15] Peiser[16] and Bruning[17] on the growth value of the various food substances, especially fats, the work of Hess[18] on scurvy, the findings of Bahrdt,[7] Edelstein and Csonka[19] regarding the iron content of human and cow's

13. Niemann, Albert: Ueber die Möglichkeit einer Fettanreicherung der Säuglingsnahrung, Jahrb. f. Kinderh., 1914, lxxix, 274.

14. Funk, Casimir: The Nitrogenous Constitutents of Lime-Juice, Biochem. Jour., vii, 81; Forschritte der experimentellen Beriberiforschung in den Jahren 1911 bis 1913, München. med. Wchnschr., 1913, lx, 1997; An Attempt to Estimate the Vitamine-Fraction in Milk, Biochem. Jour., 1913, vii, 211; Studien ueber das Wachstum, Mitteilung 1. Das Wachstum auf vitaminhaltiger und vitaminfreier Nahrung, Hoppe-Seylers Ztschr. f. physiol. Chem., 1913, lxxxviii, 352; Ueber die physiologische Bedeutung gewisser bisher unbekannter Nahrungsbestandteile der Vitamine, Ergebn. d. Physiol., 1913, xiii, 124.

15. Osborne, Thos. B., and Mendel, Lafayette, B.: Mendel, Lafayette V.: Viewpoints in the Study of Growth, Biochem. Bull., 1914, iii; The Nutritive Significance of Different Kinds of Foodstuffs, Med. Rec., New York, 1914, lxxxv, 737. Osborne, Thos. B., and Mendel, Lafayette B.: The Influence of Butter-Fat on Growth, Jour. Biol. Chem., 1913, xvi, 423; The Influence of Codliver Oil and Some Other Fats on Growth, Jour. Biol. Chem., 1914, xvii, 401; Feeding Experiments with Fat-Free Food Mixtures, Jour. Biol. Chem., 1912, xii, 81; Further Observations on the Influence of Natural Fats Upon Growth, Jour. Biol. Chem., 1915, xx, 379.

16. Peiser, J.: Ueber Fettaustausch in der Säuglingsernährung, Berl. klin. Wchnschr., 1914, li, 1165.

17. Brüning, Hermann: Untersuchungen ueber das Wachstum von Tieren jenseits der Säuglingsperiode bei verschiedenartiger künstlicher Ernährung, Jahrb. f. Kinderh., 1914, lxxix, 305.

18. Hess, Alfred F., and Fish, Mildred: Infantile Scurvy: The Blood, the Blood Vessels, and the Diet, Am. Jour. Dis. Child., 1914, viii, 385.

19. Edelstein, F., and Csonka, F. v.: Ueber den Eisengehalt der Kuhmilch, Biochem. Ztschr., 1912, xxxviii, 14.

milk, the theories of Friedenthal[20] regarding the need of sufficient *"Bausteine der Kernstoffe,"* are all of the greatest importance to the solution of the problem of a more perfect and complete adaptation of an artificial food to human breast milk, and must receive full consideration. While various mixtures have been prepared with the object of taking into account the work of some of the authors just mentioned, the present presentation aims to confine itself mainly to the analytical, bacteriologic, physical, mechanical, practical and few clinical data obtained in the work with the preparation of our so-called G-R milk No. 2, which represents nothing more or less than Friedenthal's milk in which butter fat has been replaced with another fat having about the same per cent. of low volatile fatty acids as breast milk has, and having in addition other characteristics more similar to breast milk fat than to cow milk's fat. Some analytical data regarding the fats of G-R milk Nos. 3, 4, and 5 will also be presented as well as the experience of the authors with butter washed according to Niemann.

PART I

Homogenization

A. Homogenizer.—The machine procured for us by the Walker-Gordon Laboratory was a Manton-Gaulin machine with a pressure capacity for 500 kilograms. Its liquid capacity was found by us to be about 200 c.c. The pressure used by us was 250 kilograms.

B. Technic Carried Out in the Homogenization of Various Mixtures.—(*a*) Fats—butter fat, lard, cocoanut oil, cocoa butter, codliver oil: The various fats were weighed out in sterile granite dishes. The dishes with the fats were put into a steam jacketed kettle of hot to boiling water until the contents became liquid. The pans containing the fat were then emptied and drained into a larger steam jacketed kettle into which all the other ingredients of the food had been mixed. The amount of fat remaining in the pans after thorough draining was so small as to be negligible.

(*b*) Sugar: The lactose was at first added in the form of a sugar solution of 19 to 21 per cent. Later on it was found more convenient and more accurate to simply weigh the lactose in the sterile granite pan and dump it into the common mixing kettle.

(*c*) Salts: The salts were accurately weighed in a glass receptacle. The contents of the receptacle were dumped into the mixing vat and the particles adhering to the inside of the dish rinsed out with distilled water. This amount, of course, was deducted from the batch of distilled water measured for the entire quantity.

(*d*) Skimmed milk: The amount of required skimmed milk was added to the mixture in cubic centimeters. To save time different granite pitchers were carefully marked for definite amounts.

(*e*) Water: The amount of required distilled water, less 200 c.c. for the capacity of the machine, was measured in cubic centimeters and added to the

20. Friedenthal, H.: Ueber Säuglingsernährung nach physiologischen Grundsätzen mit Friedenthal'scher Kindermilch und Gemüsepulvern, Berl. klin. Wchnschr., 1914, li, 727.

mixture. To save time different granite pitchers were carefully marked for definite amounts.

(*f*) Quantity: The amount most frequently used by us for an individual batch was 30 liters.

(*g*) Mixing: 1, mixing before homogenization: Inasmuch as the largest steam jacketed kettle at our disposal could comfortably hold but 20 liters, the fat, salt, sugar, skimmed milk, and enough water to make about a total of 20 liters were put into the vat, stirred vigorously, and brought by steam heat to a temperature of 150 F. In order to avoid an excessive loss of the fat, which would occur if the mixture were allowed to go through the homogenizer undisturbed, it was necessary to keep up a constant stirring. Soon it was possible to develop a special technic in this respect that enabled a constant mixture of the fat with the other parts of the batch. At a time when nearly all of the 20 liters had passed through the homogenizer, the remaining water was poured into the vat and run through the machine.

Recently another larger receptacle has been used for mixing all of the milk and water at one time. Out of this receptacle the milk and water mixture is run in desired amounts into the steam jacketed kettle containing the sugar, the fat, and salts. The use of this extra receptacle has lessened the time and made the practical part of the work more simple.

2. Mixing after homogenization: From the above, it will be recognized that the first part of the mixture going through the homogenizer is much more concentrated than the second part. Therefore, it is essential that a mixture of all these parts be brought about before bottling. This was managed by pouring from one can to another.

Recently we have been pouring all of the homogenized milk into the same receptacle in which the water and skimmed milk had been mixed before homogenization. This also is more simple and saves time.

(*h*) Temperature: The temperature of the mixture is brought to 150 F. before it is allowed to go through the homogenizer. It is easy to keep the batch at this temperature by regulating the steam going through the kettle and the cold skimmed milk and water coming out of the large mixing receptacle. The temperature of the milk rises about 8 to 10 degrees in the process of homogenization. During the filling, bottling, capping, etc., it drops again to about 145 to 135, and it usually enters the ice box at this temperature.

(*i*) Bottling: From the large mixing vat the milk is run into a small enamel bottling machine and filled into bottles sterilized in an autoclave. The bottles are then capped with a simple cap and with a cover cap and placed in the ice box.

(*j*) Cleanliness: All of the bottles, dishes, and utensils are sterilized in the autoclave. The mixing vat is sterilized by allowing the water to boil in it. The homogenizer is cleansed and, in all probability, sterilized by running this boiling water through it just before the homogenization of the milk is to take place. This procedure also gives one the opportunity of testing the machine for any leaks.

No more than the usual precautions are taken with the packing, shipping, etc., of the fats, sugar, skimmed milk and water.

The hands of the individuals making the milk are simply cleaned with soap and water.

The authors are aware that Friedenthal requires that the skimmed milk be not heated. They have, however, felt that for their present work, at least, it would be better and safer practically to pasteurize the finished product. In all probability there will be no difficulty when the time comes to add at least a big part of the skimmed milk in a raw state to the finished product.

PART II

Butter Fat

A. Creamery Butter.—(*a*) Cold water washing: Fresh, sweet creamery butter, in packed and in granular form, was vigorously and thoroughly rubbed and washed with some eight to ten changes of cold water. The acidity of the wash water was determined by the use of phenolphthalein and a tenth-normal sodium hydroxid solution. The amount of acids washed out was so small as to be insignificant.

(*b*) Hot water washing: Assuming that hot water might give better results, the butter was melted and the fat separated from the curd by passing through a cheesecloth. The filtered liquid was poured, together with hot distilled water, into a large bottle. The mixture was kept hot by placing the bottle in a water-bath. After thorough shaking the bottle was replaced in the water-bath and the fat allowed to separate from the wash water, which was then siphoned off for determination of its acidity. Four washings were carried out with each batch. Records of the amounts of tenth-normal sodium hydroxid required to neutralize the acids of the combined wash waters have been lost, but it can be stated that the amounts were so small as to be absolutely insignificant, and were, in all probability, due to the presence of a small amount of free acids and also caseinogen, which was being dissolved out. Burr and Weise[21] report that fresh butter fat always has a small amount of free fatty acids in amounts that require for 10 gm. of butter 0.6 to 1.4 c.c. tenth-normal sodium hydroxid solution. The best proof that the reduction in the low volatile fatty acid content of the butter was very insignificant is the finding for the same of a Reichert-Meissl number of 28, practically the same obtained in ordinary unwashed butter.

Grimmer[22] in his abstract of Niemann's article, criticizes Niemann's procedure and states that it is impossible to wash the low volatile fatty acids out of the butter because they are present in it in the form of glycerids, just as the higher acids are, and are, therefore, not free. In other words, Grimmer's statement corresponds with our findings.

(*c*) Alcohol washing: 263 gm. of clear butter fat were removed from one pound of fresh creamery butter, 255 c.c. of redistilled alcohol were added and the materials brought to boiling under thorough mixing. The mixture was then cooled to a low temperature and the alcoholic liquid decanted from the solid fat. The solid fat was then heated until the alcohol in it had evaporated. The residue weighed 252 gm. The Reichert-Meissl value of this residue fat was 4.0, and the iodin value 38.9. The addition of 10 gm. of sesame oil to 100 gm. to this alcohol washed fat gave an iodin value of 44.3. In other words, it is possible to remove the glycerids of the low volatile fatty acids from butter fat by washing with hot alcohol. The same plan has been carried out by Hunziger and Spitzer.[23]

(*d*) Emulsification according to Niemann: Both the cold water and the hot water washed butter fat were added to Friedenthal's milk in amounts to bring the fat content up to 4.5 per cent. The mixture was brought to the boiling point and was vigorously stirred, as directed by Niemann. The results were not the same as those obtained by Niemann, for the fat on standing and cooling rose to the surface. Niemann, however, used an entirely different mixture,

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21. Burr, A., and Weise, H.: Ueber den Gehalt frischen Butterfettes an freien Fettsäuren und flüchtigen Fettsäuren, Molkereizeitung, Hildesheim, 1914, No. 16.

22. Grimmer, W.: Die Arbeiten auf dem Gebiete der Milchwissenschaft und Molkereipraxis im Jahre, 1914, I Semester, Monatschr. f. Kinderh., Referate, 1915, xiv, 81.

23. Hunziker, O. F., and Spitzer, G.: A Study of the Chemical Composition of Butterfat, and its Relation to the Composition of Butter, Proc. Indiana Acad. Sc., xxv, 15.

which contained 50 gm. of mondamin (cornstarch) to each liter of milk, and this addition to his milk mixture was, in all probability, responsible for the difference in our results.

(*e*) Clinical data: Owing to the fact that the homogenizer was a very large machine used for the homogenization of large quantities of cream and was too large and unhandy for our work, and owing also to the climatic conditions that existed at that time — heat, August, 1914 — only a few older, well babies were put on the milk simply to get a rough idea how the children would take it and react to it; that is, whether there would be an improvement over Bahrdt's[5] experiences or not. Only three older infants were put on Friedenthal's milk with cold water washed butter and two on Friedenthal's milk with hot water washed butter. Two of the former reacted with thin, yellow stools in increased numbers and one vomited severely. One of the latter reacted in the same manner. The mothers of these children were not enthusiastic about our giving their babies this "new milk" under such conditions, and we, therefore, because of this and the further reasons for limiting the number of babies in the first place, decided to discontinue our clinical investigations until the arrival of cooler weather and of the smaller homogenizer, which the Walker-Gordon Company was having made for our use. The impression that we gained from this very meager experience with Friedenthal's milk and water washed butter was that there was no improvement over the results obtained by Bahrdt with the regular Friedenthal's milk.

B. Process Butter.—Process butter was considered by us because of its cheapness and also because of the fact that it surely had ample chance to decompose and so have many of the low volatile fatty acids in a free state, which condition would enable us to remove the latter by washing the butter with water. The work with this material was soon dropped because of our inability to rid it from the very disagreeable odor.

PART III

Mixed Fats, Animal and Vegetable

A. General Statement.—As stated in the introduction, our main object was to find a fat or combination of fats that would be more similar to breast milk fat than cow's milk fat, especially regarding the low fatty acid content, and to see whether a substitution of such a fat for the cow's milk fat in Friedenthal's milk might not improve this milk and represent a further step in the more complete adaptation of artificial food to human milk.

B. Experimental Data.—The accompanying table by Arnold[12] (Table 1) directed our attention to the use of lard and cocoanut oil:

TABLE 1

FROM ARNOLD'S WORK, "UEBER FRAUEN MILCHFETT"

	Cocoanut Oil	Lard	Mixture	Woman's Milk Fat, I
Refraction	35.1	47.7	47.65	47.6
Saponification number.	259.0	197.5	206.1	206.08
Reichert-Meissl number	9.0	0.4	3.0	2.65
Iodin number.....	8.5	53.0	46.77	46.25
Polenske number.....	15.8	0.15	1.65	1.65

For many reasons it seemed worth while to try to make cod-liver oil a part of this fat combination. In order to make such a mixture more palatable cocoa butter was added. We, therefore, prepared four batches of fats in the following manner:

No. 2. Lard 86.00 per cent., cocoanut oil 14 per cent.

No. 3. Lard 74.88 per cent., cocoanut oil 14 per cent., codliver oil 11.11 per cent.

No. 4. Lard 63.78 per cent., cocoanut oil 14 per cent., codliver oil 11.11 per cent., cocoa butter 11.11 per cent.

No. 5. Lard 74.88 per cent., cocoanut oil 14 per cent., cocoa butter 11.11 per cent.

It was our intention to use all four of these, but for practical reasons, after having found out that infants would take any one of them, we decided to limit our experiences for the beginning to G-R milk No. 2.

Table 2 gives first, the character numbers of the individual fats; second, the character numbers of the fats of G-R milk Nos. 2, 3, 4, and 5, obtained by calculation on the basis of the character numbers actually found for the individual fats (the individual fats were mixed by heating at 60); third, the character numbers of the fats mixed in the same proportion as they were mixed in the milk; fourth, the character numbers for the mixture of lard and cocoanut oil in the proportion as they were used in G-R milk No. 2, and heated for the same period of time as required to extract the fat from G-R milk No. 2; and fifth, the character numbers of the fat extracted from G-R milk No. 2.

TABLE 2.—DATA CONCERNING VARIOUS FATS USED

	Reichert-Meissl	Polenske	Iodin	Saponification
Lard	0.08	0.49	63.07	195.5
Cocoanut oil	6.436	13.69	8.836	259.5
Cocoa butter	0.34	0.30	36.35	196.4
Codliver oil	0.27	0.315	170.0	189.9
Mixed fats:				
(Same proportions)				
As Milk II (calculated)	0.9698	2.337	55.45	204.5
As Milk II found	1.638	1.231	55.46	206.8
As Milk II found*	2.524	1.22	.....	.....
Fat from Milk II	2.72	1.2	55.0	206.0
(Same proportions)				
As Milk III (calculated)	0.9914	2.318	66.24	203.8
As Milk III found	2.09	1.288	67.5	205.1
(Same proportions)				
As Milk IV (calculated)	1.188	2.297	63.14	204.0
As Milk IV found	2.127	1.498	64.49	205.4
(Same proportions)				
As Milk V (calculated)	0.8128	2.318	52.52	204.6
As Milk V found	1.971	1.301	52.75	206.3

* Fats in same proportion as in Milk II heated with ether for same period of time as required to extract fat from milk.

Table 2 reveals the fact that it is possible to calculate the iodin and the saponification values of mixtures of fats before or after homogenization in milk, from a consideration of these values in the individual fats. The data with equal clearness show that the Reichert-Meissl and Polenske numbers may not be so calculated, but that the mixing of the fats produces a change in the relative amounts of soluble and insoluble fatty acids that will volatilize with steam in the time required for the determination. It is noteworthy that the total amount of the volatile fatty acids is not greatly changed, for the sum of Reichert-Meissl and Polenske numbers as found is in each case approximately the same as the sum of the calculated values. This variation is not now understood and further work will be done to determine the cause of the change in value.

The slight increase of 0.2 in the Reichert-Meissl number of the fat from G-R milk No. 2 over the mixture of the same fats in the same proportions and heated for the same period of time as required to extract the fat from G-R milk, is probably due to the 0.4 per cent. of butter fat present in the skimmed milk, as can be seen from Table 5.

By comparing the character numbers as given in Table 2 for G-R milk No. 2 with Arnold's figures for his mixture and for his woman's milk fat No. 1, it will be seen that the Reichert-Meissl and saponification numbers are nearly identical; that there is a slight difference between the Polenske numbers, and a decided difference between the iodin numbers. The difference between the iodin numbers is due to the high iodin value of the batch of lard used in our work (G-R milk, lard 63.07; Arnold, lard 53.0). By rearranging the mixture we could have procured an iodin value for the G-R milk fat which would have been closer to Arnold's figures for woman's milk fat, but by doing so we would have changed the Reichert-Meissl and the saponification numbers; but as the Reichert-Miessl value seems of first importance to us, we decided to continue to use this mixture without any further change, and it is, of course, probable that a fair increase in the iodin number above that found in woman's milk fat is of no great importance.

The following figures given by Arnold[12] for his analysis of another woman's milk fat (*Frauenmilchfett No. 2*),

Refraction	48.75
Saponification	205.0
Reichert-Meissl	1.5
Iodin	45.65
Polenske	1.45

show, as one, of course, would expect, that fat from milk coming from different women will show variances in the character numbers of their respective fats.

Merkel[24] reports the following as character numbers of a butter made from the cream of a four-day quantity of milk from a wetnurse:

Saponification number	209.3
Reichert-Meissl number	1.5
Polenske number	2.2
Iodin number	46.8
Refraction at 40°	46.3

Table 3 shows that by making use of tallow—which one might imagine from Osborne and Mendel's[15] work, might even have an added value over lard—in the fat mixture, a greater resemblance as regards iodin numbers can be obtained.

24. Merkel, Eduard: Zur Kenntnis des Frauenmilchfettes, Pharm. Zentralhalle, 1912, liii, 495.

TABLE 3.—CHARACTER NUMBERS OF INDIVIDUAL FATS

	Saponification	Reichert-Meissl	Iodin
Lard	195.29	0.08	63.1
Tallow	196.6	0.5	41.4
Cocoanut oil	259.5	6.43	8.8
Cocoa butter	196.4	0.34	36.3
Codliver oil	189.9	0.27	170.0

MIXTURE WITHOUT CODLIVER OIL

	Per Cent.	Saponification	Reichert-Meissl	Iodin
Lard	50	205.48	1.07	47.36
Tallow	35			
Cocoanut oil	15			

MIXTURE WITH CODLIVER OIL

	Per Cent.	Saponification	Reichert-Meissl	Iodin
Tallow	45	205.46	1.285	45.17
Lard	15			
Cocoanut oil	15			
Cocoa butter	20			
Codliver oil	5			

Table 4 shows the materials used for a typical batch of G-R milk No. 2. The table is analyzed to show the origin of the various contributing substances:

TABLE 4.—MATERIALS FOR G-R MILK No. 2

	Total	Per Cent.				
	gm.	Water	Salt	Protein	Fat	Lactose
Skimmed milk	9,890	27.23	0.2184	0.96	0.132	1.463
Water	19,800	60.07	.....	.....	.....	.....
KCl	27	.....	0.0819	.....	.....	.....
K_2HPO_4	13.5	.....	0.0409	.....	.....	.....
KH_2PO_4	13.5	.....	0.0409	.....	.....	.....
Lard	1,274.5	.....	.....	.....	3.867	.....
Cocoanut oil	207.5	.....	.....	.....	0.629	.....
Lactose	1,740	0.0425	.....	.....	.....	5.235
Totals	32,966	87.34	0.382	0.96	4.628	6.698

The distribution of the substances from the skimmed milk shown in Table 4 is based on the analysis of the milk used, shown in Table 5.

TABLE 5.—DISTRIBUTION OF SUBSTANCES FROM SKIMMED MILK

SKIMMED MILK JUNE 18

Water	90.51
Ash	0.728
Protein	3.2
Fat	0.44
Lactose	4.87

The composition and characters of the G-R milk No. 2 prepared from the batch given in Table 4, as determined by analysis, are summarized in Table 6.

TABLE 6.—COMPOSITION AND CHARACTER OF G-R MILK No. 2

ANALYSIS

Water	87.21
Ash	0.378
Protein	0.93
Fat	4.617
Lactose	6.65

General characters: Specific gravity 15.5°, 1.032; specific conductivity 20°, 3.41 × 10^{-3} recip. ohms; freezing point depression 0.618°; caloric value per kg., 739.6 cal.

Characteristics of fat content: Size fat globules, 0.2-1 micron; brownian movement vigorous; Reichert-Meissl value, 2.72; Polenske number, 1.2; iodin number, 55.0; saponification number, 206.0.

That the milk maintained the same general composition may be judged from the accompanying analyses made at different periods (Table 7).

TABLE 7.—ANALYSIS OF G-R MILK NO. 2, AT DIFFERENT PERIODS

	May 18	May 20	June 5	June 18
Water	86.8	87.14	87.44	87.21
Ash	0.43	0.37	0.37	0.378
Protein	1.1	0.97	0.91	0.93
Fat	4.52	4.58	4.6	4.617
Lactose	7.07	6.63	6.51	6.65

The somewhat low protein and lactose content is due, in a part at least, to the fact that the milk was added as grams instead of c.c.

TABLE 8.—BACTERIAL COUNTS FOR SKIMMED AND FINISHED MILKS

Date		Count	Skim, Count
May 6	No. 2 II	Sterile	.....
May 6	No. 2 III	Sterile	.....
May 6	No. 2 IV	Sterile	.....
May 6	No. 2 V	Sterile	.....
May 12	No. 2 II	3,100	.....
May 12	No. 2 III	5,000	.....
May 12	No. 2 IV	16,100	9,850
May 19	No. 2	1,850	.....
May 20	No. 2	4,500	55,300 *
May 21	No. 2	6,000	91,000 *
May 22	No. 2	Sterile	11,300 *
May 24	No. 2	Sterile	19,700 *
May 25	No. 2	Sterile	.....
May 26	No. 2	Sterile	39,000 *
May 27	No. 2	Sterile	5,500 *
May 31	No. 2	Sterile	.....
May 29	No. 2	4,900	.....
June 2	No. 2	1,000	2,400
June 4	No. 2	Sterile	7,200
June 5	No. 2	300	8,400
June 7	No. 2	Sterile	157,200
June 9	No. 2	Sterile	6,800
June 11	No. 2	1,700	4,500
June 12	No. 2	9,000	2,000
June 14	No. 2	3,100	42,000
June 16	No. 2	Sterile	70,000
June 19	No. 2	200	3,200
June 20	No. 2	700	400
June 25	No. 2	200	300
June 26	No. 2	300	2,700

* Not certified skim.

Table 8 gives the bacteriological counts for the skimmed milk and for the finished milks, and shows on the whole very low bacterial counts for the prepared milk. These excellent results are, in all proba-

bility, due to the fact that, unknowingly, practically the same technic and conditions were established by us as advocated by Ayers and Johnson.[25]

Analytical Methods.—Water, Ash, Protein: The methods used for determining water, ash and protein are those of the A. O. A. C. described in Bulletin 107 of the Department of Agriculture.

Fat: The usual methods for fat extraction and estimation are completely unreliable with homogenized milk of this type. When the Babcock centrifugal method is used a definite separation of fatty from acid layer cannot be obtained. Various determinations were made by the Adams paper coil method, and the following figures obtained on milk that by more accurate analysis was shown to contain 4.5 per cent. of fat: 3.75, 3.69, 3.34, 2.24 per cent. A modification of the Werner-Schmidt acid method yielded fairly close results, but very great difficulty was experienced in securing a separation of the acid and ether layers. The Roese-Gottlieb process was then employed, and it was found that excellent results can be obtained when low-boiling petroleum ether (35 C.) is used, and the second and third extractions accomplished by inversion, without shaking, of the mixture. The above recorded analyses substantiate the accuracy of this method.

Method of Fat Extraction from Milk: 150 c.c. of milk were diluted with 250 c.c. water, and 9 c.c. of 1 per cent. sulphuric acid added, with constant stirring. A cylindrical cup made from fat-free filter paper was fitted closely into a Buchner funnel and after moistening the paper the acidified mixture was filtered. After normal filtering had ceased, the filtrate was discarded and suction applied until most of the water was removed. This final filtrate was shaken with ether, and the ether subsequently used for the extraction of the fat from the precipitate. The filter paper with precipitate was transferred to a mortar and ground with about 20 gm. anhydrous sodium sulphate, when a dry, somewhat waxy porous powder resulted. This powder was placed in a Soxhlet apparatus, where extraction was complete in two hours. The ether was then driven off, or in some cases the ether solution was transferred by pipet to the vessel in which a determination was to be made.

Reichert-Meissl Value: Leffmann and Beam's saponification method was used, and the distillation continued thirty minutes.

Polenske Number: Glycerol saponification was used, and the condenser tubes washed three times with water, then three times with alcohol.

Iodin Number: The Wjis method was used.

Saponification Number: One gm. of the fat was saponified with 5 per cent. potassium hydroxid in specially purified alcohol. It is of importance that the blank determination be heated on the water bath for the same period of time as the regular determinations.

Size of Fat Globules: The value of 0.2 to 1 microns was roughly approximated by the use of Thoma's hemacytometer. The fat globules exhibit remarkable uniformity of size, and all show vigorous brownian movement.

Lactose: The solid lactose used was examined both polarimetrically and by reduction, and found to be 99.2 per cent., $C_{12}H_{22}O_{11}.H_2O$. Lactose in milk was determined in each case by the polarimeter, using acid mercuric nitrate for precipitation, and estimating the solids by the method of double dilution. To check the polarimetric method, the milk analyzed on June 18 was determined also by the reduction method, using Soxhlet's modification of Fehling's solution, weighing the copper as cupric oxid, and calculating lactose from the

25. Ayers, S. H., and Johnson, W. T., Jr.: Pasteurization in Bottles and the Process of Bottling Hot Pasteurized Milk, Jour. Infect. Dis., 1914, xiv, 217.

Soxhlet-Wein tables. The results show the absence of any substances in the milk that would vitiate the accuracy of the polarimetric method.

Per cent. lactose by polariscope 6.51
Per cent. lactose by reduction 6.537

Specific Gravity: Quevenne's lactodensimeter was used at 15.5 C.

Conductivity: Conductivity was measured by the Kohlrausch method, using a cell with electrodes about 1 cm. apart and 2.5 cm. in diameter.

Depression of Freezing Point.—The determination was made by the usual method. It is highly important that the temperature of the freezing mixture be not lower than about —1.5 C. as the concentration of the solution by the settling out of ice changes the f. p. significantly.

Calorimetry: To determine the heating value, 2 c.c. of milk were accurately weighed in a small combustion cup. This was placed in a desiccator equipped with shelves holding dishes filled with calcium chlorid. Evacuation was accomplished by a water pump, and in twenty-four hours the material had dried and showed no evidence of loss by spattering. The dried milk was then burned in a Parr bomb with 20 atmospheres oxygen pressure. The calculation of heating value from the analysis of milk reported in Table 7 (June 18) closely agrees with the direct calorimetric determination.

	CALCULATION FROM ANALYSIS	
Protein	0.93 × 5.85	5.44 C.
Fat	4.617 × 9.1	42.02 C.
Lactose	6.65 × 3.96	26.33 C.
		73.79 C. per 100 gm. milk
Obtained from calorimeter		73.96 C. per 100 gm. milk

C. Clinical Data.—(*a*) Vomiting: The clinical experience until now has not been sufficient to be considered worthy of report. It is hoped at a later time to present the clinical results. A statement, however, can be made regarding the degree of vomiting and dyspeptic stools met with so frequently by Bahrdt in his patients fed with Friedenthal's milk prepared with unchanged cow's fat. Of a list of twenty babies, from 1 week to 7 months of age, there was spitting up or slight vomiting in five. In two of these this has disappeared; in a third, the vomiting continues once a day; and in the other two there still exists a slight vomiting. Two other children showed marked vomiting before they were put on the food; the one gradually improved while on the milk, and now does not vomit at all, and the other is a case of pylorospasm which continues to vomit, but which has begun to gain in weight since it has been getting the food.

(*b*) Stools: Of the twenty children only two showed dyspeptic stools. Two were constipated and passed rather firm, somewhat formed, fatty soap stools. The remainder had what we termed normal stools. These varied in color from a lemon-yellow to an orange-yellow, were of a lard-like, pasty consistency, and contained, in most instances, smaller or larger masses of soft, fatty soaps. Many of the stools changed from a yellow to an olive-green in the diaper.

These few data suffice to prove that the vomiting has been decidedly less and the stools decidedly more normal in our children than they were in Bahrdt's, and we believe that this is due to the removal of the low volatile fatty acids. Whether the fact that the milk was homogenized has anything to do with these better results is impossible to say at the present time. Birk, according to Grulee,[26] could find no improve-

26. Grulee, Clifford G.: Infant Feeding, W. B. Saunders Co., 1912.

ment in the children by homogenizing their foods. On the other hand, Lavialle[27] believes that the homogenization greatly enhances the digestibility of a milk because it offers to the digestive ferments a much larger action surface, and because it causes, by reason of the marked brownian movement, the formation of currents, which are responsible for an active mixing of ferments and foods. Inasmuch as the fat in human milk does not exist in such a fine emulsion as the fat of homogenized milk, it can at least be assumed that a finer division than is present in human milk is not necessary; on the other hand, there is, at present, no reason to believe that any harm is done to the fat or any other constituent of the milk by homogenization, excepting, of course, the effect of the raised temperature on some of the constituents of skimmed milk; and it may be found that homogenization is of greater value in the production of artificial human milk than the mere mixing for which it has been used by us.

(*c*) Weight: The following figures are given to show that normal or slightly below normal infants made good gains in weight. Eighteen infants, from 1 week to 7 months of age, for a total period of seventy-three weeks, made a total gain of 10,630 gm., or an average of 145 + gm. per week.

D. Economical Data.—Friedenthal's milk made up with a mixture of fats like lard, tallow, cocoa butter, cocoanut oil, cod-liver oil, olive oil, cottonseed oil, sesame oil, and the like, can be produced at a price decidedly lower than when butter freed from a large per cent. of its low fatty acid glycerids is used. The cost of the fat per liter of various combinations with various fats, is as follows:

For a mixture of tallow 40 per cent., lard 10 per cent., cocoanut oil 20 per cent., cocoanut butter 20 per cent., codliver oil 10 per cent.	1.30 cents
G-R Milk No. 2	1.43 cents
G-R Milk No. 3	1.60 cents
G-R Milk No. 5	1.70 cents
G-R Milk No. 4	1.80 cents
Friedenthal's milk with cow's butter fat, without considering the cost of washing the butter with alcohol	3.70 cents

While the production cost of a milk for infants is not of the first importance, yet it is, nevertheless, true that there are many families who cannot get for their infants what they should have simply because of the price, and, therefore, if an adequate food can be prepared at a low cost it is an advantage that is important when it is desired that all families whose infants require it should get it. It is also interesting to think of the economy that would result in a general way by the reduction in the use of the more expensive butter and the increase in the use of fats that are distinctly cheaper.

27. Lavialle, P.: Le mouvement brownien dans le lait homogeneise, Clin. infant., 1913, xi, 490.

SUMMARY

1. By mixing varying proportions of different animal and vegetable fats, it is possible to get a fat that in its Reichert-Meissl number (small per cent. of low volatile fatty acid glycerids), saponification number, iodin number, and other characters, is nearly identical with the fat of human milk, as has previously been shown by Arnold.

2. By replacing in an artificial milk cow's-milk fat with the fat of the above description in an emulsified state (homogenized), a distinct step in advance towards the more complete adaptation of an artificial food to breast milk is made.

3. It is also possible to take into consideration the "growth factors," "vitamine factors," and the like, in choosing the individual fats for an acceptable mixture. This represents a further step in the more complete adaptation of an artificial milk to human milk.

4. The homogenizer represents the important means by which the mixing and emulsification of the fat in the artificial milk is possible. The homogenizer also changes the physical condition of the fat (smaller globules, brownian movement), which may be of advantage.

5. The meager clinical data suffice to show that the infants fed with Friedenthal's milk in which the cow's-milk fat has been replaced by a fat with a low volatile fatty acid glycerid content, similar to that of human milk fat, vomit less and have more normal stools than the children reported by Bahrdt, and fed with Friedenthal's milk containing unchanged cow's-milk fat.

6. Washing butter with cold or hot water does not remove the low volatile fatty acids from butter, except in an insignificant degree.

7. Washing butter with hot alcohol does remove the low fatty acid glycerids to a decided degree.

8. The manufacture of a food like G-R milk can be arranged to give a very low bacteriologic count.

9. The production of milk like G-R milk can be made at a reasonable cost.

EXTENSIVE PURPURIC ERUPTIONS IN EPIDEMIC MENINGITIS *

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Since epidemic meningitis was first described as "spotted fever" a great deal of just criticism has been directed against the term. Even the earliest writers admit that skin manifestations occur in a comparatively small percentage of the cases—too small, indeed, to justify the use of the title.

In his treatise on "A Malignant Epidemic Commonly Called Spotted Fever," North[1] draws attention to the fact that in the 1806-1807 epidemic in Massachusetts, skin eruptions were very common, while in the later epidemic of 1808-1809 they were almost never observed. "The size of the lesions varied from the head of a pin to a six cent piece and the distribution was more commonly on the face, neck and extremities." He believed that the color of the rash was a guide in prognosis; that is, the darker the shade the more hopeless the outcome.

In the Ireland epidemic in 1867, nearly every case showed skin manifestations. Gordon[2] reports several such cases and gives a very accurate description of the various forms of eruption.

Frew,[3] in 1884, describes seven cases during an epidemic in Scotland, three showing hemorrhagic eruptions; of these three, only one was purpuric. He believed, however, that there were numerous patients showing no eruption who recovered, and these he was not sure were the same disease.

In the Massachusetts epidemic in 1866, Webber[4] reports that 33 per cent. of the cases showed petechiae; only a few, however, were purpuric. Here also the color of the rash was considered to be an aid in prognosis.

This is in striking contrast to the epidemic in the same state in 1898, during which, according to the investigation by Councilman, Mallory and Wright[5] only eleven cases out of 111 showed eruption of any kind, and in only one was there a true extravasation into the skin.

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* Submitted for publication July 21, 1915.

1. North, Elisha: A Treatise on a Malignant Epidemic Commonly Called Spotted Fever, T. and F. Swords, New York, 1811.
2. Gordon: Dublin Quart. Jour. Med. Sc., 1867, xliii, 408.
3. Frew, William: Glasgow Med. Jour., 1884, xxii, 21.
4. Webber, S. G.: Boston Med. and Surg. Jour., 1866, lxxv, No. 2, p. 29.
5. Councilman, Mallory and Wright: Report of State Board of Health of Massachusetts, Boston, 1898.

In a series of fifty cases occurring in New York city reported by Conner[6] in 1905, only 5 per cent. showed any eruption, and in a more recent outbreak in Texas, which was so thoroughly investigated by Sophian,[7] hemorrhagic eruptions were uncommon and true purpura extremely rare, being found in less than 1 per cent. of the cases.

These reports suggest that in the early history of the disease, skin eruptions were more frequent than have been observed recently. This is probably due to the fact that other forms of the disease were not recognized as they are today.

The two following cases are reported as examples of very unusual skin lesions in epidemic meningitis:

REPORT OF CASES

CASE 1.—F. H., aged two years, was admitted to the Babies' Hospital, Feb. 6, 1914, at 10 a. m.

Fig. 1.—Taken on the fourth day of the disease, showing eruption on buttocks and lower extremities, Case 1.

History.—There was no family history of hemophilia or any hemorrhagic disease and the child himself had never been sick before. The patient was well up to twenty-four hours before admission, when he seemed listless, appeared feverish and refused food. The only medication the child had received was twelve tablets of calomel, size unknown. At 11 p. m. the same day he seemed better and fell asleep. Two hours later the child awakened screaming and the mother then observed that the face was covered with a black eruption. On removing the bedclothes the eruption was discovered also over the extremities. This, she declared, had not increased up to the time of admission to the hospital. There had been no vomiting, no convulsions, and only slight fever. Stools were green and loose, but not tarry, and the urine was normal in color.

Examination.—On examination was found a well developed and nourished child, evidently severely ill, in a condition of semistupor, with marked pros-

6. Conner, L. H.: Med. News, 1899, lxxiv, 685.

7. Sophian, Abraham: Epidemic Cerebrospinal Meningitis, C. V. Mosby & Co., St. Louis, 1913.

tration. Did not respond to stimuli such as noises; was apparently deaf and blind; periods of drowsiness alternated with periods of restlessness and screaming. The child was extremely hyperesthetic when handled and was particularly so when the legs were moved. No opisthotonos was present but the neck was slightly stiff; knee jerks exaggerated; Kernig's sign, not elicited; pupils equal and reacted normally; no strabismus or conjunctivitis; tache cérébrale present. Respirations rapid but regular; examination of the lungs revealed nothing abnomal. Heart sounds were rapid and slightly feeble; the pulse small and thready, but regular; spleen not enlarged; slight general enlargement of superficial lymphatic glands in cervical, axillary, inguinal and epitrochlear regions; the nodes were soft, small and discrete.

Large blotches of purpura were found on the face, extremities and buttocks interspersed with petechiae of varying sizes. The intervening skin was blanched white and the combination presented an appearance which was ghastly; the child looked as though splashed with a quantity of black ink. The eruption was to some extent symmetrical in that it involved both sides of the

Fig. 2.—Taken on the fourth day of the disease, showing eruption on face and outer side of thighs, Case 1. Note the absence of lesions on the trunk.

face, both shoulders, the extensor surfaces of the arms, the buttocks and outside of the legs. The largest areas were found on the face, on the elbows, buttocks and thighs, one on the right thigh measuring 6 inches in length. The distribution did not appear to correspond to any particular nerve or vascular supply, but the fact that it was extensive over the elbows and buttocks suggested a possible traumatic etiology. The trunk, except for a few small petechiae, remained clear. The conjunctivae and the mucous membrane of the mouth and throat showed no eruption. The center of the larger patches was purple in color, the periphery was reddish brown, and surrounding this was a zone of hyperemia. There was a distinct elevation above the normal skin level. In some cases this subcutaneous infiltration seemed to correspond with the edge of the purpuric patch but this was not invariable, as the induration could be felt under normal skin in the immediate neighborhood of the larger hemorrhages. The areas of purpura seemed acutely tender and the skin of the whole body was hyperesthetic. The photographs shown in Figures 1 and 2 were taken on February 8 and give an idea of the widespread distribu-

tion of the eruption; Figure 2 shows very well the absence of the lesions on the trunk.

Subsequent Course.—The eruption did not spread during the day, but the temperature which on admission had been only 100 F., rose abruptly to 102.8 and the child vomited twice very forcibly. The leukocytes were 40,000 per c.mm. with 75 per cent. polymorphonuclears; hemoglobin 80 per cent.; platelets in moderate numbers found in the stained smear; coagulation time of the blood (specimen taken from vein and Duke's instrument used) was forty-five minutes; bleeding time, two and one-half minutes. Macroscopic, microscopic and chemical tests failed to show blood in either urine or feces. A slight internal strabismus of left eye developed during the day; ophthalmoscopic examination showed no papilledema and no retinal hemorrhages. Ears normal. Cultures were taken from the blood and from the purpuric patches. Lumbar puncture was performed and 20 c.c. of blood-tinged fluid was obtained which was cultured in various mediums.

Fig. 3.—Taken on the twelfth day of the disease, Case 1, showing the disappearance of many of the smaller lesions. The commencing separation of the gangrenous tissue is easily discernible at the margin of the larger areas.

The following day the patient was much less irritable and the screaming attacks less frequent. The muscles of the neck and back were more rigid; Kernig's sign absent. Leukocytes 22,000 per c.mm. with 78 per cent. polymorphonuclears; temperature ranging between 101 and 104. Coagulation time of the blood had dropped to twenty minutes; the eruption had not spread or changed in appearance. A second lumbar puncture gave 25 c.c. of turbid fluid, which was removed under increased pressure and showed on examination 4,000 cells per c.mm., of which 92 per cent. were of the polymorphonuclear variety. A direct smear of the fluid showed a very few intracellular and extracellular gram-negative diplococci; 20 c.c. antimeningitis serum were injected intraspinally.

The progress of the case from this point need not be given in detail. The child received intraspinal injections of the serum every day for three days, the size of the injection being controlled by the fluctuations in blood pressure. The cerebrospinal fluid became gradually less turbid; the cell count dropped to 350 per c.mm. on the sixth day of the disease and to 86 per c.mm. on the ninth day.

The leukocytes were estimated every day and ranged between 16,000 per c.mm. and 20,000 per c.mm. with a gradual drop in the polymorphonuclear percentage. The blood culture taken on February 6 showed in thirty-six hours a growth of meningococci; the organisms could not, however, be demonstrated in the culture taken on the following day. Spinal fluid cultures showed a faint growth of the same organism. Cultures from the purpuric patches remained sterile four days.

The mental condition of the child gradually improved, the vomiting ceased and the rigidity of the neck diminished. A transient right facial paralysis was noticed on February 9, which disappeared on the following day. The temperature after the eighth day of the disease ranged between 100 and 101 F. until the termination of the case.

The course of the eruption was so unusual as to deserve a more detailed description.

The rash on the fifth day of the disease showed a gradual change in color, the center of the larger areas became paler and the outside rim took on a rose-colored tint. On the sixth day one or two of the larger patches showed a central area, grayish-black in color, which had a consistency like cardboard. On the ninth day the smaller purpuric patches began to desquamate, leaving a depressed pigmented scar. The petechiae had also disappeared, leaving only a brown pigmentation. Two days later sloughing commenced at the margin of several of the larger areas of ecchymosis on the body, the excavation in some places extending down to the muscle. The child's breath became very foul due to a separation which had commenced at the left margin of the ecchymosis on the nose. The necrosis penetrated to the nasal passages and through the sinus there was a profuse discharge of fetid mucopus, which was of a very foul and typically gangrenous odor. The photograph shown in Figure 3 was taken February 16 and illustrates the commencing slough at the upper margin of the lesion on the right thigh and hip. Comparison of Figures 1 and 3 shows the disappearance of the petechiae and smaller purpuric spots.

The necrosis continued until the gangrenous tissue had in some localities completely sloughed out leaving a large ulceration lined with unhealthy granulations. The entire tip of the nose became necrotic on the fifteenth day and was removed, exposing the nasal bones. The character of the lesions at this period bore a striking similarity to the extensive symmetrical gangrene seen in severe cases of Raynaud's disease.

The child's condition became progressively worse, the symptom complex being one of general sepsis. The temperature rose to 106.5 on February 22, the seventeenth day of the disease, and the child died the same day. Repeated convulsions occurred during the twenty-four hours previous to death; an exacerbation of the meningitis was suspected, but the cerebrospinal fluid on February 20 was found to be normal.

Necropsy.—An autopsy was performed on February 22 by Dr. Wollstein. With the exception of a superficial strip of bronchopneumonia along the posterior border of the right lower lobe, and a small hemorrhage on one cusp of the aortic valve, the thoracic and abdominal organs were normal. The pia mater at the base of the brain was turbid, but there was no exudate; the vessels of the pia everywhere were congested, most markedly so over the left cortical surface. The ventricles were not distended and contained a small amount of very slightly turbid fluid; the brain substance was congested. There was congestion of the pia mater along the entire length of the spinal cord but no sign of exudate. In short, the findings were those of a recovered case of epidemic meningitis.

CASE 2.—M. O., female, aged 15 months, was admitted to Babies' Hospital, June 11, 1915.

History.—A previously healthy child except for an attack of pneumonia in January, 1915, and measles in April, 1915; both diseases terminated without complication after running a perfectly normal course.

The mother's story was that on June 8 the child became abruptly ill with vomiting and fever. About eighteen hours later a rash suddenly appeared on the face and extremities; the mother declared she "could watch the spots coming out." The vomiting continued up to admission and the stools were loose and dark green in color. The infant had been listless, but there had been no convulsions.

Examination.—Examination revealed abnormalities only in the nervous and cutaneous systems. The child was slightly apathetic, irritable when handled and markedly hyperesthetic; acutely ill but not prostrated. Pulse and respirations regular. Very slight spasm on attempted flexion of the head on the chest; Kernig's sign absent; patellar reflexes, not exaggerated; tache cérébrale marked; ocular movements normal.

Fig. 4.—Taken on the eighth day of the disease, Case 2, showing eruption over outer surface of legs and thighs.

Scattered over the face, the upper and lower extremities and the buttocks was a hemorrhagic eruption. The majority of the lesions were purpuric, only a few petechiae being present. The spots were of various sizes and shapes, the largest being 13 mm. in length. On the extremities the lesions were found more commonly on the extensor surfaces. The trunk except for a few small spots over the scapular region was clear. The lesions were discrete and the larger ones elevated above the skin level, with a marginal induration of the subcutaneous tissues. The mucous membranes of the mouth and throat were normal; one small hemorrhage found on left conjunctiva and several retinal hemorrhages were revealed by an ophthalmoscopic examination. The larger ecchymoses had a purple center surrounded by a rose red areola, the intervening skin being much paler than normal.

The character, color and distribution of the eruption bore so striking a resemblance to the eruption in Case 1 as to suggest, in spite of the absence of the usual signs of meningeal involvement, the diagnosis of epidemic meningitis.

This diagnosis was corroborated by examination of the cerebrospinal fluid. Fifteen cubic centimeters of purulent fluid were obtained under increased pressure; the cell count was 22,500 per c.mm., 88 per cent. of the cells being of the polymorphonuclear variety. A direct smear of the sediment showed moderate numbers of gram-negative diplococci.

Course.—The progress of the case from this point may be briefly summarized: The child received 15 c.c. antimeningitis serum intraspinally on four successive days; the cells in the cerebrospinal fluid showed a gradual diminution in number, so that on June 15 the count was only 660 per c.mm. with 10 per cent. polymorphonuclears, and on June 19, 107 per c.mm. with 2 per cent. polymorphonuclears. Positive cultures of meningococci were obtained from the fluid taken at the first and fourth punctures. Blood culture obtained June 12

Fig. 5.—Taken on the eighth day of the disease, Case 2, showing a few of the larger lesions on left leg.

also showed a sparse growth of the same organism. The leukocyte count on June 12 was 18,500 per c.mm. with 80 per cent. polymorphonuclears; with each succeeding day there was a drop in the polymorphonuclear percentage, but the total count continued to range between 16,000 and 23,000 per c.mm.

The general improvement of the patient was immediate and striking, rigidity of the neck disappeared and she was able to sit up in bed unassisted six days after admission. The petechiae on June 21 had almost disappeared, nothing being visible but a faint brown pigmentation. Absorption of the subcutaneous hemorrhage around the larger areas was complete by June 21, and the lesion was at this time represented by a depressed scar capped by a reddish brown crust. Figures 4 and 5 are from photographs taken after the smaller lesions had almost disappeared and show a few of the larger individual lesions.

The child's recovery was complete and uncomplicated, she was discharged on June 30 and has continued to improve up to the time of writing.

DISCUSSION

Unusual features of the two cases with additional facts of interest:

1. The character and distribution of the eruption, which was unlike the usual purpura hemorrhagica and which though differing greatly in degree was almost identical in both patients.

2. Paucity of other meningeal signs, such as opisthotonos and other manifestations of increased muscle spasm.

3. Demonstration of the specific organism in the blood of both patients, though attempts to grow the same organism from the skin lesions were unsuccessful.

4. Refutation of the old theory that the extent and color of the eruption was of prognostic aid. In both the above cases the meningeal manifestations were no more marked than usual, and were quite amenable to treatment.

5. Both cases were sporadic as far as could be learned by investigation of the locality and by a study of the Board of Health daily bulletin.

I am indebted to Dr. Holt, on whose service the cases were observed, for permission to publish this report.

THE TONSILLAR MANIFESTATIONS IN THE EARLY DIAGNOSIS OF MEASLES*

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What one does not look for one does not see. This is well illustrated in the case of the oral manifestations of measles. The disease is extremely common; numerous careful observers have examined innumerable patients and still the significance of certain manifestations for a long time escaped detection. I can find only three authors who have mentioned the tonsillar spots as an early manifestation of measles. Comby[1] reported four cases of measles in one family and described white spots (*angine pultacée*) as being present on the tonsils of two of these cases two days before the eruption appeared. Grumann[2] describes white spots or streaks about 3 mm. long which are present on the tonsils one or two days before the eruption. Miller[3] reports the case of a child which, when first examined, besides a rise of temperature, had dyspnea and a reddened throat. The tonsils were swollen and on each tonsil there were a number of small bluish semitransparent elevated bodies averaging considerably less than the size of the head of an ordinary pin. The eruption appeared the following day. No Koplik's spots were observed.

It is interesting to note that occasionally when these spots on the tonsils were seen, they were regarded as merely coincidental and their relation to the onset of measles not recognized. To cite one example, in von Pirquet's splendid monograph on measles two of Friedjung's cases are quoted to illustrate an unusually long period of incubation:

> The first patient was taken sick on May 17, with a temperature of 39 C., apparently due to an angina lacunaris. May 18, 37.8 C., no change in the child's condition. May 19, 38.6 C., Koplik's spots and catarrhal symptoms. May 20, 39.5 C., beginning eruption. On June 2, the twin brother of the patient still showed no symptoms. On June 3, the temperature was 38.5 C. and there was an "angina lacunaris"; there were also a few indistinct Koplik's spots near the outlet of Stenson's duct. On June 4, 37.8 C. and an enanthema on the hard and soft palate. June 5, 38 C., no change. June 6, 39.6 C., beginning eruption.

* Submitted for publication July 15, 1915.

1. Comby: Arch. de méd. des enf., 1900, p. 420.
2. Grumann: München. med Wchnschr., 1914.
3. Miller: Bull. Johns Hopkins Hosp., 1914, p. 78.

In both of these patients the tonsillar spots were present three days before the eruption, and in the first patient two days before the Koplik's spots.

In a paper recently published,[4] I mentioned that in ten cases of measles which I had seen in the early stage, four had presented the tonsillar spots, and that in two of these their appearance had preceded the Koplik's spots. During a recent epidemic I have had an opportunity to study this manifestation more carefully. Including the ten cases mentioned, I have now notes on 88 cases seen in the early stage; that is, at the beginning of the invasion. In eighty cases (90 per cent.) Koplik's spots were observed, in thirty-five cases (40 per cent.) the tonsillar manifestations were present. I should like to emphasize the fact that the patients must be seen in *the early stage, and the spots*

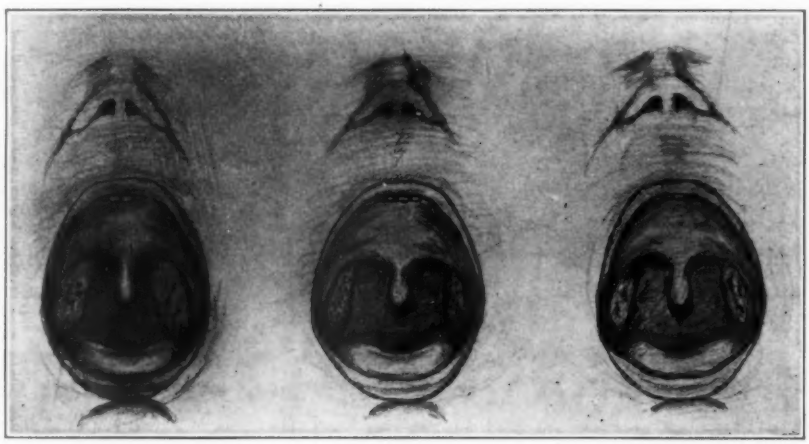

Figure 1 Figure 2 Figure 3

Tonsillar spots seen in the early stages of measles. Fig. 1.—A few round spots about the size of the head of a pin. Fig. 2.—A large number of very small spots or streaks. Fig. 3.—A few irregular streaks.

must be looked for. A good light is essential, the tongue must be depressed, and the tonsils must be examined. The tonsillar spots vary in number, size, shape, and color. There may be only two or three, or there may be twenty or thirty; they vary in size from the point to the head of a pin; they occur as round spots, as very small regular or larger irregular streaks (Figs. 1, 2, 3). The color seems to depend on the thickness, and varies from a bluish gray to white. They are seen only in the very early stage of the disease, and are visible one or two, occasionally three days. They are more frequently seen on enlarged

4. Herrman: Arch. Pediat., 1914, p. 885.

and succulent tonsils. The tonsils, as well as a small mass of lymphoid tissue on the soft palate just above and to either side of the uvula, frequently become hypertrophied at this stage of the disease. In the 35 patients in whom the tonsillar spots were observed, in 9 patients they were present one day before the eruption appeared; in 11 patients two days, in 7 patients three days, in 5 four days, in 2 six days, in 1 nine days before the eruption appeared.

In 30 of the 35 patients Koplik's spots were observed, in 14 patients one day before the eruption appeared, in 15 two days, in 1 three days before the eruption appeared.

In 13 patients the tonsillar spots were seen one day before Koplik's spots; in 3 two days, in 2 three days, in 1 four days, in 1 seven days before Koplik's spots.

In 5 patients the Koplik's spots were seen 1 day before the tonsillar; in 5 patients the Koplik's spots were seen on the same day as the tonsillar spots, and in 5 patients the Koplik's spots were not seen, so that the interval could not be determined.

In 12 patients the spots were visible for one day; in 17 two days, in 6 for three days.

At the time when the spots were first seen, the temperature was less than 100 in 6 patients, between 100 and 100.5 in 6, between 100.5 and 101 in 3, between 101 and 101.5 in 8, between 101.5 and 102 in 2, between 102 and 102.5 in 7, between 102.5 and 103 in 1, and between 103 and 103.5 in 2 patients.

It will be noted that in two-thirds of the patients the temperature was not over 101.5 at the time when the spots were first observed. This fact serves as a valuable point in differentiating the spots from those of follicular tonsillitis. In the latter the temperature is usually higher, the prostration is more marked, and there is usually an absence of catarrhal symptoms. In this disease also as the spots disappear the temperature falls; in measles, on the other hand, after the tonsillar spots disappear the temperature rises.

Not infrequently measles begins with an attack of croup and diphtheria may be suspected. If the tonsils show any spots, the suspicion may be increased; but in cases of measles the examination of the culture will be negative, and the rise in temperature and the increase in the catarrhal symptoms will clear up the diagnosis. In such cases, a knowledge of the appearance of the tonsillar spots of measles will be a valuable aid in differential diagnosis.

Taken altogether the tonsillar spots are much less valuable in the early diagnosis of measles than the Koplik's spots, first because they are present in only about 40 per cent. of the cases, and secondly,

because their appearance is not always so characteristic that they can be easily differentiated from those of follicular tonsillitis; but in families, classes, hospital wards, asylums in which other cases have occurred, or in which the disease is epidemic, it may be a very valuable aid in isolating the patients *early*. These spots are frequently present when the child has no other objective symptom except a slight rise of temperature.

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THE TOTAL NONPROTEIN NITROGEN AND THE UREA OF THE BLOOD, AND THE PHENOLSULPHONEPHTHALEIN EXCRETION IN CHILDREN *

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The total nonprotein nitrogen of the blood has not been studied in children, so far as we are aware, and the urea of the blood has been determined only by the somewhat crude hypobromite method, to which, as Rowntree and Fitz[1] have shown, an error of from 10 to 60 per cent. attaches. We have therefore thought it worth while to investigate the blood in this respect, in various diseases of childhood and in healthy children. We have also investigated the phenolsulphonephthalein excretion, using the method of Rowntree and Geraghty. Owing to the small material available, the series is far from complete.

The term "nonprotein nitrogen" is synonymous with incoagulable nitrogen, rest or waste nitrogen and retention nitrogen, and designates the nitrogen of those substances remaining after the removal of the proteins. It includes the urea, creatinin, amino-acids, uric acid, and ammonia of the blood.

Technic.—For the nonprotein nitrogen and the urea nitrogen the methods of Folin and Denis[2] have been followed. Only a small amount of blood, from 2 to 5 c.c., is required. The blood was drawn from a vein of the arm or from the external jugular vein by means of a syringe. Whole blood was used, clotting being prevented by means of potassium oxalate. The figures are calculated in terms of milligrams of nitrogen per hundred cubic centimeters of blood. The values obtained for urea nitrogen include the ammonia nitrogen, which, however, is so small in amount in normal blood, and presumably in most cases of disease, as to be negligible.

In performing the phenolsulphonephthalein test, or as it will be called henceforth, for short, the phthalein test, the directions of Rowntree and Geraghty[3] were followed. The urine was obtained by catheter in every instance, the catheter being held in place by strips of adhesive plaster. This is necessary in the case of young children

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* From the Department of Medicine, Yale University Medical School.
* Read at the meeting of the American Pediatric Society, Lakewood, N. J., May 24, 1915.

1. Rowntree, L. G., and Fitz, R.: Arch. Int. Med., 1913, xi, 258.
2. Folin, O., and Denis, W.: Jour. Biol. Chem., 1912, xi, 527.
3. Rowntree and Geraghty: Jour. Pharm. and Exper. Therap., 1909, i, 579.

who will not urinate on command, and for the sake of uniformity of results, was done also in the case of the older children. The urine was collected separately for each of the first two hours after the injection, and the amount of the dyestuff was estimated in each of the two specimens.

The nitrogen and the urea determinations were made by Tileston, the phthalein estimations by Comfort.

Total Nonprotein Nitrogen and Urea Nitrogen in Healthy Children.—At first we took the blood in the morning, just before the noon meal, an arrangement which has proved satisfactory in the case of healthy adults, who show at this time from 22 to 26 mg. nonprotein nitrogen, about half of which is in the form of urea nitrogen.

We found in children, however, as will be seen by glancing at Table 1, a considerable variation at this time of day, in one case up to 34 mg. of nitrogen. We were led, therefore, in the case of children over 2 years of age, to take the blood before breakfast after a fast of twelve hours or more. In the two cases examined at this time there were 24.4 and 26 mg. of nitrogen and 9.5 and 10.9 mg. of urea nitrogen, respectively. The urea is seen to form somewhat less than one-half of the total nonprotein nitrogen, while if the influence of diet is not eliminated, the urea may constitute considerably more than one-half the total.

The influence of diet must therefore always be borne in mind in this kind of work, though in the case of children who are acutely sick, and taking in consequence less than the accustomed amount of food, we have found that the blood may be taken at any time of day without the liability of error.

The Phenolsulphonephthalein Excretion in Healthy Children.—The phthalein excretion in normal children has been found to vary from 35 per cent. to 64 per cent. for the first hour, and from 17 per cent. to 44 per cent. for the second hour. These wide variations are eliminated, however, if the total excretion for the two hours be considered, the figures then falling within very narrow limits, from 78 to 81 per cent. It is therefore evident that no conclusions can be safely drawn from this test unless the period of observation is extended to two hours. For practical purposes it will be sufficient to collect the urine for two hours in one vessel and make one determination of the phthalein.

The phthalein excretion in healthy children is considerably higher than in the adult, where values anywhere from 50 to 80 per cent. are considered normal.

A word of explanation is necessary in connection with the urine examinations in Table 1. The presence of red cells and a slightest

possible trace of albumin is accounted for in some instances by the fact that a catheter has been passed previously. In other cases it is the normal albuminuria which can usually be demonstrated in health by the nitric acid test, if done by an expert.

Acute Nephritis.—Owing to the small size of the clinical material, we have but three cases of nephritis to report, all acute. The first was a case of scarlatinal nephritis in a girl 8 years old. The history was vague, fever having been remarked a week before entrance to the hospital, and swelling of the feet five days later, but no rash. The diagnosis was cleared up later by the appearance of typical desquamation of the feet. Mild uremic symptoms were present, such as prostration, drowsiness and vomiting. The eyelids were puffy, but there was no edema elsewhere. The examination of the urine indicated an acute nephritis of considerable severity, showing 0.3 per cent. albumin, with many brown granular and hyaline casts, red blood corpuscles and leukocytes. Both the nitrogen and the urea were markedly increased, the former measuring 64 and the latter 43 mg. The phthalein excretion was 39 per cent. in two hours. A month later the nitrogen had fallen to normal and the albumin to a very slight trace, and she was discharged well soon afterward.

The second case was one of unknown origin and moderate severity, in a boy 9 years old. The only symptoms were puffiness of the face and albuminuria. The urine showed a large trace of albumin, with many blood and granular casts, red blood cells and leukocytes. There was a slight elevation of the blood nitrogen (34.5 mg.) and of the urea (21 mg.). The phthalein output was 56 per cent. in two hours. The albumin dropped in a few days to a slight trace, the casts and red cells being still numerous. He was discharged at the end of two weeks with only the slightest possible trace of albumin and a few casts.

The third case occurred as a complication of lobar pneumonia, in a boy 30 months old. He entered the hospital on the eighth day of the disease, the crisis occurring next day. There was a large trace of albumin in the urine, with hyaline, granular and epithelial casts, and red blood cells. The blood nitrogen and urea were normal and the phthalein excretion over 54 per cent. (some urine lost). Five days later the albuminuria had nearly disappeared and he was discharged well soon after. This case might be regarded as one of febrile albuminuria by some, on account of its prompt subsidence, but the large amount of albumin, together with the frequency of nephritic changes (especially glomerulonephritis) at postmortem examinations of such cases, would appear to justify the diagnosis.

The cases, so far as they go, indicate that nephritis when accompanied by uremic symptoms tends to show a marked increase in the

TABLE 1.—NORMAL CASES *

Name	Case No.	Sex	Age	Diagnosis	Phenolphthalein			Urine			Diet	Blood		Remarks
					Per Cent. in 1st Hr.	Per Cent. in 2d Hr.	Total in 2 Hrs.	Sp. Gr.	Alb.	Microscopical		Total N, Mg.	Urea N, Mg.	
Leissenhaltz..	1	M	7	Fractured leg.....	64	17	81	1.031	S. P. T.	Many W. B. C. and R. B. C.	Mixed...	20.2	10.5	Blood taken at noon.
Juliano.....	2	M	9	Fractured arm....	58	20	78	1.020	S. P. T.	Negative.....	Mixed...	24.4	9.5	Blood taken fasting.
Ferraro.....	3	M	4½	Fractured femur..	35	44	79	1.025	S. P. T.	Negative.....	Mixed...	26.0	10.9	Blood taken fasting.
Melillo.....	4	M	3	Burn of eye.....	52	27	79	1.030	S. P. T.	W. B. C.	Mixed...	31.9	17.8	Blood taken at noon.
Dest.	5	M	3	Phimosis.....	..	..	..	1.018	0	Negative.....	Mixed...	34.0	19.6	Blood taken at noon.

* The following abbreviations are employed in this and following tables: S.P.T. = slightest possible trace; V.S.T. = very slight trace; S.T. = slight trace; H.T. = heavy trace; W.B.C. = white blood corpuscles; R.B.C. = red blood corpuscles; the figures for albumin were obtained by the Esbach method, and represent percentages.

TABLE 2.—NEPHRITIS

Name	Case No.	Sex	Age	Diagnosis	Day of Disease	Phenolphthalein			Urine			Diet	Blood		Remarks
						Per Cent. in 1st Hr.	Per Cent. in 2d Hr.	Total in 2 Hrs.	Sp. Gr.	Alb.	Microscopical		Total N, Mg.	Urea N, Mg.	
Faust.....	6	M	2½	Ccute nephritis, complicating acute lobar pneumonia	9	40	14+	54+	1.026	H. T.	Hyaline, granular, and epithelial casts; many R. B. C.; W. B. C.	Liquid..	26.2	13.6*	T. = 99.7 F.
									1.027	S. P. T.	Rare hyaline cast; occasional W. B. C.	.....	....	....	Five days later.
Lucibello....	7	M	9	Acute nephritis...	11	19	37	56	1.015	H. T.	Many blood and granular casts; many R.B.C. and W.B.C.	Low protein	34.5	21.0	T. = 99 F. Etiology unknown
Dunn.....	8	F	8	Acute nephritis, complicating scarlatina	4-9	..	..	39	1.010	0.3 %	Hyaline and brown granular casts; many R.B.C. and W.B.C.	Liquid..	63.6	42.9	T. = 98.6 F.
									1.013	V. S. T.	Hyaline, granular, and pus casts; R.B.C.: W.B.C.	Liquid..	31.0	....	T. = 98.6 F. thirty days later.

* One determination.

TABLE 3.—PNEUMONIA

Name	Case No.	Sex	Age	Diagnosis	Day of Disease	Phenolphthalein			Urine			Diet	Blood		Remarks
						Per Cent. in 1st Hr.	Per Cent. in 2d Hr.	Total in 2 Hrs.	Sp. Gr.	Alb.	Microscopical		Total N, Mg.	Urea N, Mg.	
Carbone....	9	F	4	Pneumonia, acute lobar	6	5	40	45	1.024	V. S. T.	Very many W.B.C.....	Soft.....	20.2	13.3	Temp. 105.4 F.
Katz.....	10	M	15mo.	Pneumonia, acute lobar	9	5	12	17		S. P. T.	Granular casts; W.B.C.	Formula	22.2	12.9*	Temp. 104 F.
Szeresnowicz	11	M	9	Pneumonia, acute lobar	5	..	..	68	1.024	S. P. T.	W.B.C.	Soft.....	23.1	11.8	Temp. 104.2 F. Crisis ended next day. Moderately severe case
													24.0	12.6*	Temp. 98.6 F.
Grauel.....	12	F	8	Pneumonia, acute lobar	..	..	..	63	1.020	V. S. T.	Occasional hyaline cast and R.B.C.; W.B.C.	Very soft	24.4	13.8	Temp. 100 F.
Rumano....	13	M	9	Pneumonia, acute lobar	11	55	30	85	1.025	S. P. T.	Occasional R.B.C.: few W.B.C.	Soft.....	24.7	10.4	Temp. 102 F.
Knudsen....	14	F	8 mo.	Pneumonia, acute lobar	8	..	..	53		S. P. T.	Rare hyaline and granular casts; few R. and W.B.C.	Formula	25.6	11.7	Temp. 102 F. Empyema later.
Malvedo....	15	M	6 mo.	Pneumonia, acute lobar	8	..	..	..		S. P. T.	Negative.....	Formula	28.3	14.6	Temp. 105 F. Died next day.
Levy.....	16	M	5	Pneumonia, acute lobar	3	..	..	70	1.020	S. P. T.	Rare hyaline cast; numerous W.B.C.	Soft.....	29.7	21.2	2/22/15. Temp. 104 F.
													27.8	15.2*	2/24/15. Temp. 99 F.
Zoufman....	17	M	8	Pneumonia, acute lobar	7	..	..	57	1.025	S. P. T.	Occasional fine granular and hyaline cast and R.B.C.; W.B.C.	Soft.....	32.6	19.8	Temp. 103 F.

TABLE 4.—SCARLATINA AND TYPHOID FEVER

Name	Case No.	Sex	Age	Diagnosis	Day of Disease	Phenolphthalein			Urine			Diet	Blood		Remarks
						Per Cent. in 1st Hr.	Per Cent. in 2d Hr.	Total in 2 Hrs.	Sp. Gr.	Alb.	Microscopical		Total N, Mg.	Urea N, Mg.	
Russell.....	18	M	7	Scarlatina.....	5 da.	..	..	..	1.028	0	Negative..... ..	Soft.....	21.7	10.1	Temp. 103.5 F. Moderately severe case.
Vaughn.....	19	F	10	Scarlatina.....	4 da.	..	..	..	1.018	S. P. T.	Negative.....	Soft.....	23.2	10.9	Temp. 100.8 F. Moderately severe case.
Miller.....	20	M	11	Scarlatina.....	3 da.	42	40	82	1 029	S. P. T.	W.B.C.	Liquid..	26.6	15.3	Temp. 99 F. Blood taken fasting. Mild case.
Dowd.....	21	F	7	Scarlatina.....	5 da.	..	..	74	1.032	V. S. T.	Few hyaline and granular casts, W.B.C.	Liquid..	26.7	15.1	Temp. 100.8 F. Mild case.
Koskoff, Y.	22	M	9	Scarlatina.....	3 da.	26	46	72	1.027	S P T.	W.B.C.	Liquid..	26.9	16.3	Temp. 102.8 F. Blood taken fasting. Moderately severe case.
Scandone...	23	F	17mo.	Scarlatina.....	5 da.	44	5+	49+		S. P. T.	W.B.C.	Liquid..	27.8	13.6*	Temp. 101 F. Mild case.
Cohen.....	24	F	3	Scarlatina.....	3 da.	40	34	74	1.024	S. P. T.	Fine granular casts; rare R.B.C.; W.B.C.	Soft.....	28.1	14.2*	Temp. 102.5 F. Moderately severe case.
Koskoff, L.	25	F	5	Scarlatina.....	1 da.	35	29	64	1.018	0	Negative.....	Liquid..	28.5	15.4	Temp. 101 F. Blood taken fasting. Mild case.
Weinstein...	26	F	7	Scarlatina.....	2 da.	55	31	86	1.032	0	Negative.....	Soft.....	29.1	13.8	Temp. 101 F. Moderately severe case.
Bartholemew	27	M	10	Scarlatina.....	5 da.	..	..	66	1.030	S. P. T.	Negative.....	Soft.....	31.9	....	Temp. 99 F. Mild case.
Gentile.....	28	M	3	Typhoid fever....	10 da.	31	32	63	g.n.s.	S. P. T.	W.B.C.	Typhoid	21.9	10.3	Temp.101-104F. Blood taken fasting.
Daniels.....	29	F	8	Typhoid fever....	10 da.	48	24	72	1.026	S. P. T.	Few W.B.C.	Typhoid	22.7	11.1	Temp. 104 F. Blood taken fasting.
Wilens.....	30	M	8	Typhoid fever....	7 da.?	..	..	75	1.010	V. S. T.	W.B.C.	Typhoid	22.7	11.9	Temp. 104 F.
Cruscola....	31	F	5	Typhoid fever....	5 wk.	56	8	64	1.012	S. P. T.	Occasional granular cast; few R. and W.B.C.	Typhoid	25.0*	....	Temp. 102 F.
Daddio.....	32	M	5	Typhoid fever....	8 da.	21+	36+	57+	1.028	S. T.	Occasional fine granular cast; R.B.C.	Typhoid	29.0	14.2	Temp. 99-102 F.
Gladwin.....	33	F	10	Typhoid fever....	12 da.	..	..	71	1.020	V. S. T.	Hyaline casts; few R.B.C.; W.B.C.	Typhoid	29.2	15.8	Temp. 103 F.

* One determination.

TABLE 5.—Miscellaneous Diseases

Name	Case No.	Sex	Age	Diagnosis	Day of Disease	Phenolphthalein			Urine			Diet	Blood		Remarks
						Per Cent. in 1st Hr.	Per Cent. in 2d Hr.	Total in 2 Hrs.	Sp. Gr.	Alb.	Microscopical		Total N, Mg.	Urea N, Mg.	
Brazen.....	34	M	3½	Diphtheria.....	1 da.	..	..	..	1.020	0	Negative.....	Liquid..	25.3	13.9	Temp. 102.8 F. Mild case.
Peck.....	35	M	8	Diphtheria.....	3 da.	61	15	76	1.020	S. P. T.	Few hyaline casts and W.B.C.; rare R.B.C.	Liquid..	28.4	14.1	Temp 99 F. Severe case. Complicated later by myocarditis.
Sinclair.....	36	F	8	Pertussis.....	3 wk.	24	6	30	1.026	0	Occasional W.B.C.	Liquid..	23.6	11.0	Temp. 102.4 F. Complicated by bronchopneumonia.
Campagne..	37	F	6	Tuberculous neck glands	3 mo.	51	19	70	1.026	S. P. T.	Few W.B.C.	Mixed...	24.4	....	Temp. 99 F. Blood taken fasting.
Frabianna..	38	F	3	Tuberculous peritonitis	6 wk.	..	..	63		S. P. T.	Few granular casts and R.B.C.; many W.B.C.	Soft.....	27.2	12.0	Temp. 98-102 F.
Daniels.....	39	F	8	Tuberculous hip..	1 yr.	..	..	84	1.022	S. P. T.	Rare R.B.C.; W.B.C...	Soft.....	27.2	....	Temp. 98.6 F.
Ryan.....	40	M	5	Tuberculous hip and spine	..	38	45	83	1.032	0	Negative.....	Soft.....	32.0	17.3	Blood taken fasting.
Masorka....	41	F	13mo.	Tuberculous meningitis	2 wk.	..	..	..	.....	.....	.....	Formula	21.2	10.3	
Makarias...	42	F	18mo.	Tuberculous meningitis	1 wk.	56	23	79		S. P. T.	Many R. and W.B.C. .	.....	27.5	14.2	Temp. 102 F.
Alberino....	43	F	10	Tuberculous meningitis	5 da.	..	..	55	1.032	V. S. T.	Rare hyaline cast; W.B.C.	Liquid..	31.6	19.1	Temp. 102.8 F.
Villow.....	44	M	4	Cerebrospinal meningitis	4 da.	63	15	78	1.015	V. S. T.	Rew granular casts; R. and W.B.C.	Soft.....	25.9	11.4	Temp. 101.8 F.
Hathaway..	45	F	7	Keratitis; congenital lues	8 wk.	..	..	61	1.022	S. T.	Few W.B.C.	Mixed...	23.4	13.6	Temp. 99 F.
Lavalle.....	46	M	8	Endocarditis and pericarditis, rheumatic	..	..	..	80	1.022	S. P. T.	Few hyaline casts; W B C	Soft.....	22.7	11.0	Temp. 102 F.
Weiss.....	47	F	6½	Chorea.....	2 wk.	..	..	..	1.025	0	Negative.....	Low protein	23.6	12.1	Temp. 99 F. Blood taken fasting.
Mazzanotti.	48	M	6	Rickets.....	..	63	15	78	1.023	S. P. T.	Few W.B.C.	Soft.....	23.4	10.6	Blood taken fasting.
Rascati.....	49	M	2½	Rickets, gastroenteritis	2 mo.	43	29	72	1.016	S. P. T.	W.B.C.	Soft with extras	26.9	12.7	Temp. 102 F. Blood taken fasting.
DiYilsi.....	50	F	4	Rickets.....	..	..	..	86	1.018	0	Negative.....	Mixed...	29.7	18.1*	Temp. 99.2 F.
Ferrucci.....	51	F	8	Ichthyosis.....	8 yr.	..	..	74	1.015	S. P. T.	Many R. and W.B.C...	Mixed...	21.5	11.7	Temp. 98 F.

* One determination.

total nitrogen and urea. In the cases without uremic manifestations, on the other hand, the increase is slight or absent. The phthalein appears to vary roughly with the degree of impairment of renal function.

Acute Lobar Pneumonia.—In this disease nine out of ten patients showed no increase whatever in the total nitrogen; in the tenth case there was a trifling increase up to 33 mg. The urea was normal in eight cases, and moderately increased in two. This is contrary to our experience[4] in the pneumonia of adults, where 70 per cent. of those over 21 years of age showed more than 35 mg. of nitrogen. A fatal case in an infant of six months showed normal figures for both nitrogen and urea the day before death, as did also the case complicated with nephritis, already alluded to in the section on nephritis.

The phthalein excretion in pneumonia varied from 17 to 85 per cent. for two hours, the average being 57 per cent. The case with 17 per cent. excretion showed only a slightest possible trace of albumin and 22 mg. of nitrogen, not differing either clinically or with respect to the blood and urinary findings from the case with 85 per cent. excretion. The child with nephritis showed over 54 per cent. phthalein. These facts illustrate the danger of drawing conclusions from a single application of the phthalein test in acute conditions.

Scarlatina.—We were particularly interested in this disease, on account of the frequency with which nephritis occurs as a complication. Contrary to our expectations, we found practically normal values in all of the ten cases not complicated by nephritis, the highest figure for nitrogen being 32 mg. and the highest for urea 16 mg. The case of scarlatinal nephritis has been described already, in the section on nephritis.

The phthalein excretion in the cases without nephritis averaged 75 per cent., a much higher figure than that obtained in pneumonia (57 per cent.).

Typhoid Fever.—Six cases of typhoid fever all showed normal values for both nitrogen and urea. The phthalein excretion averaged 68 per cent.

We have also examined instances of diphtheria, pertussis with bronchopneumonia, tuberculosis of various tissues, cerebrospinal meningitis, hereditary syphilis, rheumatic pericarditis, chorea, rickets and ichthyosis; all with negative results.

CONCLUSIONS

1. The determination of the total nonprotein nitrogen and urea of the blood is of great assistance in the diagnosis of uremia, and as a guide to the treatment of nephritis, a marked increase in these sub-

4. Tileston and Comfort: Arch. Int. Med., 1914, xiv, 620.

stances indicating actual or impending uremia, and calling for a diet low in protein. In the diagnosis of nephritis it is inferior to other methods, because many cases of nephritis show no retention of nitrogen.

2. The phthalein test is very valuable in the diagnosis of nephritis, showing probably better than any one other method the degree of impairment of renal function. In the diagnosis of uremia and as a guide to diet it is inferior to blood analysis, for a low phthalein output may occur without retention of nitrogen.

3. These investigations of the blood and of the phthalein excretion would appear to indicate a better secreting capacity of the child's kidney as compared with that of the adult.

THE ATROPIN TREATMENT FOR THE EXUDATIVE DIATHESIS IN INFANCY*

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Some years ago Czerny gave the name of "Exudative Diathesis" to a group of symptoms characterized by an exudation into the skin and mucous membranes. The skin of infants suffering from exudative diathesis shows some form of eczema, varying in grade from a very mild seborrhea to extensive infiltration, with excoriation. The so-called geographic tongue is seen in some cases. Catarrhal affections of the respiratory tract—coryza, pharyngitis, recurrent bronchitis, and asthma—make their appearance. A catarrh of the gastro-intestinal tract is often present. General glandular enlargement with an enlarged spleen may be combined with one or more of the other manifestations. An eosinophilia is found in the blood examination of some of the cases. The exudative diathesis is generally encountered either in very obese or in very thin infants; some of the cases, however, are normal in weight and development.

The eczema, bronchitis and asthma occurring in infants with other symptoms of exudative diathesis are occasionally very resistant to the ordinary methods of treatment. The very fat, overfed babies are at times greatly improved by reduction in diet with consequent loss in weight. The symptoms occurring in poorly nourished infants occasionally clear up rapidly with proper regulation of the diet and gain in weight. In both classes of cases external treatment of the eczema in the form of ointments is used in combination with the dietetic therapy. With the most careful combined treatment, however, a certain proportion of the cases fail to improve. The eczema persists for many weeks, months, or even years, and there are recurrent attacks of asthma, bronchitis, and pneumonia. It is for these patients that the atropin treatment is advocated.

ATROPIN TREATMENT

Before detailing my results a brief review of the development of the atropin therapy should be given. Although the cause of the exudative diathesis is unknown,[1] Eppinger and Hess believe that it is

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1. According to Czerny, "exudative" infants are born with a constitution different from normal infants. Metabolism studies on these infants have varied a good deal, and have thrown very little light on the cause.

an infantile form of vagotonia, and various manifestations are thus due to increased tone in the vagus system. With this theory in mind, Krasnogorski treated a number of infants, ill for many months with the manifestations of exudative diathesis, with atropin, a drug causing, as is well known, decrease of vagus irritability. Six infants, all under 9 months of age, were treated. Four of them had suffered from severe grades of eczema and two from bronchitis and asthma. Cures followed administration of atropin in all these infants. No toxic effects such as flushing and dryness of the skin, dilatation of the pupils, tachycardia, etc., were observed, and Krasnogorski therefore concluded that infants suffering from exudative diathesis were very tolerant to the drug.

During the past year I have administered the atropin treatment to ten infants suffering from symptoms of the exudative diathesis—severe eczema, bronchitis or asthma. Mild cases were not treated, for I believe that the best test of the efficacy of the atropin therapy would be the advanced and pronounced cases. The patients were all institutional babies ranging in age from 4 months to 2 years, and were under constant medical supervision. Careful observations were made on the condition of the pupils, skin, pulse rate, etc. Temperatures were recorded several times daily. The infants under 1 year were weighed daily, and the older infants once or twice weekly. As the accompanying case reports will show, the results of the atropin treatment on the lesions of the exudative diathesis were excellent; and this despite the fact that no changes in diet were made, and no other drugs administered. One infant (Case 9) died during the period of observation. In this patient atropin had a beneficial effect on the eczema, but in no wise influenced the pulmonary condition, death following a terminal bronchopneumonia.

Method of Administration.—Atropin was used in a solution of 1 grain of atropin sulphate to 480 drops of water.[2] Three drops of this solution were given on the first day of treatment, and if no untoward effects were observed, the dose was increased 1 drop daily until patients received about 30 drops daily (equivalent to 1/16 grain of atropin sulphate). This last dose was given daily for one or more weeks until the manifest signs of the exudative diathesis had disappeared. Smaller doses were then administered for a few more days or weeks. In only one case (Case 2) did untoward manifestations appear; they were very mild, and did not recur after the initial dose of the atropin solution had been reduced. In no case was there any harmful result from the atropin treatment. It was clearly evident from the beginning that infants suffering from exudative diathesis

2. In one case a 1:960 solution was used.

were able to take large doses of atropin sulphate without showing toxic effects.

Whether the theory of Eppinger and Hess prove true or false, the fact remains that striking results were obtained in my series of cases by atropin treatment administered on that theory. From a study of these cases it is fair to conclude that atropin sulphate in increasing doses given over long periods of time is of great value in the treatment of those severe and obstinate manifestations (eczema, bronchitis, asthma) of the exudative diathesis which do not respond to the ordinary dietary and local treatment. It will be my further object to determine if repeated courses of atropin are required or if a single course will effect a permanent result.

CASE REPORTS

CASE 1.—Aged 11 months. One of triplets. Weight 12¼ pounds. On modified milk mixture. Evidences of rachitis. There was present a very marked generalized eczema, and an intertriginous eczema in the inguinal region, and over the buttocks. A history of recurrent attacks of bronchitis was given.

Treatment.—One drop of a solution of atropin sulphate 1:480 three times daily, increasing one drop each day. After four weeks 30 drops of the solution (1/16 of a grain) were given daily. This dose was continued for four days when slight flushing of the skin, some regurgitation of food, and tachycardia set in. The atropin was then reduced to 24 drops daily. The toxic symptoms did not reappear and the dose was kept up for ten days. Atropin was then discontinued. The eczema had entirely cleared up and there were no attacks of bronchitis. Two months later the general condition was excellent; weight 15¼ pounds, and there were no signs of the exudative diathesis.

CASE 2.—Aged 11 months. Weight 14 pounds. On modified milk mixture. There were present a marked generalized eczema, and a diffuse bronchitis.

Treatment.—The infant first received 1 drop of a solution of atropin sulphate 1:480 three times daily. With this dose there was slight flushing of the skin, dilated pupils, and a rapid pulse. One drop of a 1:960 solution was then given. There was no reaction with this dose. It was increased one drop daily until the infant was receiving at the end of forty-one days, 44 drops daily (corresponding to about 1/20 grain of atropin). This dose was continued for ten days without any reaction. The bronchitis had completely cleared up and the eczema was markedly improved after one week. One-sixteenth grain of atropin was then given for one week without any reaction. Then 1/20 grain was given for sixteen more days. The drug was then stopped. Twice during this period there were slight attacks of bronchitis which lasted four and five days, respectively. The eczema was completely controlled after eight weeks' treatment. One month after treatment had been stopped there had been no recurrences of the eczema or bronchitis.

CASE 3.—Agd 2 years. Weight 25 pounds. Regular diet. Very well developed child. There was a severe papular-vesicular eczema on both cheeks. This eruption extended around the left ear. There was a patch of eczema in the left auditory canal. There were lesions characteristic of lichen urticatus on both arms. The skin lesion had been of four months' duration and was gradually getting worse.

Treatment.—One drop of atropin solution 1:480 was given three times daily. This was increased one drop daily. After eighteen days the dose was 20 drops daily, or 1/24 grain of atropin. There was never any untoward reaction. After

three days' treatment the eczema was markedly improved, and after two weeks' treatment it had almost cleared up. There still remained a slight grade of erythema which responded to the application of silver nitrate and Lassar's paste.

CASE 4.—Aged 12 months. Weight 17 pounds. Regular diet. A severe papular eczema was present on the face and lower extremities. There was also a seborrheal eczema of the scalp.

Treatment.—Atropin sulphate, 1 drop three times daily of a 1:480 solution, was given, increasing one drop daily. After two weeks the infant was receiving 18 drops daily (3/80 grain). This dose was given for four days and then decreased 1 drop daily because the eczema showed such marked improvement. The eczema cleared up entirely after two weeks' treatment. The atropin was given for five weeks and then stopped. There had been no recurrence after two months. During the previous three and one-half months the infant gained 5½ pounds. Its general condition was excellent.

CASE 5.—Aged 7 months. Weight 16 pounds. On a simple milk mixture. Rachitic infant. Geographic tongue. Severe eczema of both lower extremities and over entire body. Face clear. Slight scaling of scalp.

Treatment.—The infant received 1 drop three times daily of a 1:480 solution of atropin sulphate, which was increased 1 drop daily until 10 drops were given daily. The atropin was stopped after fifteen days, when the eczema was completely cured. Three months after treatment had been stopped there had been no recurrence of the eczema. The infant's general condition was very good. It weighed 20½ pounds.

CASE 6.—Aged 4 months. Weight 14½ pounds. On buttermilk feedings. There was present a severe eczema of the scalp, face, and buttocks. There were many asthmatic râles present throughout both chests.

Treatment.—Infant received atropin sulphate solution in increasing doses until 16 drops were given daily. With this dose (grain 1/30 of atropin) there was slight flushing of the skin. The pupils were dilated at times. After seven days' treatment the lungs were entirely clear and the infant's general condition was much improved. The eczema was practically controlled. The atropin was discontinued after fourteen days' treatment, when all signs of eczema and asthma had disappeared. Four months after treatment had been stopped the infant weighed 17½ pounds. There had been no recurrence of the eczema or asthma. The general condition of the infant was excellent.

CASE 7.—Aged 7 months. Weight 15 pounds. On buttermilk and cereal feedings. There were present many asthmatic râles throughout both chests. There was some scaling of the scalp.

Treatment.—Atropin sulphate solution 1:480 was given beginning with 1 drop three times daily, and increasing 1 drop daily until 15 drops or about 1/30 of a grain was given daily. With this dose there was slight flushing of the skin. The dose was then reduced to 1/48 of a grain daily, and this dose was given for two weeks and then stopped. The asthma was completely cured after one month's treatment. One month after treatment had been stopped the infant had another attack of asthma. Atropin sulphate was given again, beginning with 5 drops three times daily. This dose was increased daily until the infant was receiving 30 drops, or 1/16 grain daily. The attack of asthma was cured in one week. Six weeks after treatment was stopped the infant's condition was excellent, and it had had no more attacks of asthma.

CASE 8.—Aged 15 months. Weight 23½ pounds. On regular diet. There was a history of recurrent attacks of asthma. There was some scaling of the scalp. Both chests were filled with asthmatic râles.

Treatment.—Atropin sulphate solution was given in increasing doses until the infant was receiving 1/16 of a grain daily. The asthma was completely cured in nine days. Two months after treatment had been stopped there had been

no recurrence of the asthma. The infant weighed 25½ pounds. Its general condition was excellent.

CASE 9.—Aged 11 months. Weight 14½ pounds. On regular diet. Very poorly developed infant with marked rachitis. Severe generalized seborrheal eczema. For two weeks severe diffuse bronchitis. Pirquet reaction negative. Coughed a good deal. Temperature between 98 and 103.8 F. Respirations between 28 and 80.

Treatment.—Infant received one drop of a 1:480 solution of atropin sulphate three times daily, increased one drop daily until about $\frac{1}{20}$ of a grain of atropin sulphate was given each day. After five days' treatment the eczema was somewhat better. The bronchitis remained the same. After two weeks' treatment the eczema was completely controlled, but the diffuse bronchitis persisted. During this period the infant gained 10 ounces in weight. The temperature and respirations continued about the same. Finally a bronchopneumonia developed and the infant died. In this patient atropin controlled the eczema, but had little, if any, effect on the pulmonary condition.

CASE 10.—Aged 10½ months. Weight 12 pounds. On a regular diet. Rachitic infant. No teeth. The infant had marked beading of the ribs, craniotabes and a markedly distended abdomen. Muscles flabby. The liver and spleen palpable. Geographic tongue. Marked scaling of the scalp. Severe papular eczema of chest. Intertriginous eczema of folds of neck. Very severe asthma of both chests. Temperature between 98.6 and 101.6 F.

Treatment.—One drop of atropin sulphate solution (1:480) was given three times daily until the infant was receiving about $\frac{1}{30}$ grain of atropin daily. With this dose there was at times dilatation of the pupils and slight flushing of the skin. One-thirtieth grain of atropin was given daily for a period of three weeks, and was then discontinued. The infant's condition gradually improved under atropin treatment. After sixteen days' treatment the eczema was controlled and the lungs were almost clear. After five weeks' treatment the eczema had entirely disappeared and the asthma was cured. During the atropin period the infant gained 2 pounds in weight.

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PROGRESS IN PEDIATRICS

EXUDATIVE DIATHESIS—A REVIEW*

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HISTORICAL

The idea of the diatheses is very old (His[1] and Krehl[2]). It played a prominent rôle in the medicine of ancient Greece, especially the school of Galenus, and it persisted up to the beginning of the modern scientific study of the natural phenomena, when exact examination took the place of philosophic speculation and when Virchow's cellular pathology and the widespread use of the microscope dislodged the constitutional theory.

At the beginning of the present century the German school of medicine resurrected these old theories, which had always been adhered to by the French, and medical writers in Europe, especially in these two countries, have given ample expression to the ideas of disposition and constitution. In pediatrics as well as in dermatology these theories have helped us to understand many a clinical picture which would otherwise have remained veiled.

THE DIATHESES

The term diathesis attempts to give expression to the internal relations of heterogeneous groups of diseases, due to individual conditions, which are usually congenital, often hereditary. In these physiologic stimuli cause an abnormal reaction and morbid phenomena under normal conditions of life.

At present we are able to recognize only certain groups of symptoms, to which we give the name of a diathesis; such as arthritism, lithemia, exudative diathesis, spasmophilia, status thymicolymphaticus, mongolism, infantilism, eosinophilia, some neuropathies, hemophilia; perhaps also epilepsy, chlorosis and the hypoplasias of the aortic system (His[1]).

The French school of medicine recognizes the *diathèse arthritique*. This they regard as a disease of the intellectual classes, of those with sedentary habits, and therefore a disease of degenerating races.

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1. His, W.: Geschichliches und Diathesen in der inneren Medizin, Deutsch. med. Wchnschr., 1911, xxxviii, 857.
2. Krehl, A.: Med. Klin., 1911, vii, 752.

Comby[3] considers arthritism as a morbid temperament which is dormant in childhood and does not appear until adult life; in childhood, however, the symptoms of the hereditary taint will be observed under the guise of imperfect nutrition, incomplete development, hypertrophies or hyperplasias, a defective arterial system, and an abnormal and easily vulnerable connective tissue.

Hutinel[4] states that it is, at present at least, very difficult to define arthritism. It is not a disease, but a morbid temperament, a peculiar form of metabolism.

De Monchy[5] thinks that arthritism and exudative diathesis should be clearly separated, even more so than has been done by Czerny.

Galup[6] brings arthritism in relation to anaphylactic phenomena.

In English and American medicine we find under the name of lithemia the symptoms which French writers collect under arthritism, Rachford.[7] Others, for instance Whitmore,[8] describe under lymphatism the status thymicolymphaticus, or they recognize this latter condition only, as for instance Holt.[9]

The majority of the writers in the English language, however, fail to mention the diatheses altogether. This neglect is now beginning to be recognized. Cameron[10] deplores this fact and shows the importance of the diatheses on infant feeding and infant mortality.

Dutch literature is also rather wanting on the subject of the diatheses. Some, like Sthemann,[11] refuse to recognize their revival, while others, like Gorter,[12] take a standpoint somewhat between the French and German schools.

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3. Comby, J.: Arthritisme; Grancher et Comby, Traité des Maladies de l'Enfance, Paris, 1904, i, 770.

4. Hutinel, V. and Tixier, L.: Arthritisme.—Etat lymphatique. In V. Hutinel's Les Maladies des Enfants. Volume 2, pages 612 and 688, Paris, 1909, ii, 612.

5. de Monchy: Diathesen bei Kindern, reviewed in Jahrb. f. Kinderh., 1911, lxxiv, 468.

6. Galup, J.: Le lymphatisme. Diathèse d'anaphylaxie-immunité. Une conception générale des diathèses, reviewed in Ztschr. f. Kinderh., 1913, Referate, v, 668.

7. Rachford: Lithaemia, Arch. Pediat., August, 1897: Symptomatology of Lithemia, Arch. Pediat., September, 1897.

8. Whitmore, A.: Lymphatismus in the East, Lancet, London, 1911, clxxxi, 752.

9. Holt, E.: Diseases of Infancy and Childhood, Ed. 5, New York, 1910.

10. Cameron, H. C.: On Diathesis in Infancy; a Plea for Its Closer Study, Brit. Med. Jour., 1914, p. 53.

11. Sthemann: Konstitutionsanomalien bei Kindern., Jahrb. f. Kinderh., 1911, lxxiv, 576.

12. Gorter, E.: Ueber exsudative Diathese, Lymphatismus and skrophulöse Konstitution, reviewed in Jahrb. f. Kinderh., 1911, lxiii, 271.

Since the memorable paper of Czerny,[13] published ten years ago, in which he first mentioned the name of *exudative diathesis,* many monographs have been published on the subject of the diatheses, and their importance in medicine has, by some at least, been fully appreciated.

Some German authors, like Pfaundler,[14] consider it a mistake to confound diathesis with dyscrasia, and the symptoms of a diathesis with the diathesis itself.

Von Behring[15] confines the term diathesis to only a small part of the disposition. He considers a diathesis as an individual, congenital, often inherited condition, in which physiologic stimuli cause an abnormal reaction.

Klotz[16] considers the status lymphaticus to be an extreme type of exudative diathesis.

Sittler[17] states that exudative diathesis is found so frequently in children nowadays that one might feel inclined to regard these symptoms merely as the physiologic reaction to the unhygienic mode of living now prevailing.

Pfaundler[18] considers the diatheses of childhood, namely, exudative diathesis of Czerny, status thymicolymphaticus of Paltauf, infantile arthritism of Comby, to represent identical conditions, viewed only from different standpoints.

ETIOLOGY

Friedjung[19] is a strong believer in Adler's theory of organic inferiority. Constitutional differences are then the reason why infants may fail to thrive under the best of care, even with well-regulated breast feeding; also why vastly different methods of artificial feeding may give either good or bad results in the hands of the same investigator.

Lederer[20] finds the cause of exudative diathesis in the water metabolism.

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13. Czerny, A.: Die exsudative Diathese, Jahrb. f. Kinderh., 1905, lxi, 199.
14. Pfaundler, M.: Kindliche Krankheitsanlagen (Diathesen) und Wahrscheinlichkeitsberechnung, Ztschr. f. Kinderh., 1912, iv, (Orig.) 175.
15. v. Behring, E.: Disposition und Diathese, reviewed in Ztschr. f. Kinderh., 1914, Referate, viii, 273.
16. Klotz, M.: Die Bedeutung der Konstitution für die Säuglingsernährung, Würzburg. Abhandl. a. d. Ges. d. prakt. Med., 1911, xi, 181.
17. Sittler, P.: Die exsudativ-lymphatische Diathese, Würzburg, 1913.
18. Pfaundler, M.: Zur Lehre von den kindlichen Diathesen oder Krankheitsbereitschaften, reviewed in Jahrb. f. Kinderh., 1911, lxxiv, 486.
19. Friedjung, J. K.: Die Enährungsstörungen der Brustkinder und Konstitution, reviewed in Ztschr. f. Kinderh., 1913, Referate, iv, 595.
20. Lederer, R.: Exsudative Diathese und Wasserstoffwechsel, Ztschr. für angewandte Anat. u. Konstitutionsleiden, 1914, 1, 233.

Steinitz and Weigert[21] have made repeated metabolism experiments on two infants and they have found decreased nitrogen and fat metabolism.

Riesel[22] found that out of thirty-five children whose bodily conditions were marked on their history charts as fat or pasty, twenty-six had most of the symptoms of exudative diathesis.

Maillet[23] considers the subcutaneous tissue to be of the greatest importance for the nutrition as well as the defense of the body.

Mendelsohn[24] is an adherent of Bouchard's[25] theory of the retardation of metabolism and of humoral hypo-acidity.

Pässler[26] has a rather remarkable, though not convincing, view of the etiology of exudative diathesis. He finds this, as well as other related diatheses, to be always caused by chronic streptococcus infections of the buccal cavity, especially caries dentium and pyorrhea. He claims that thorough cleansing of the mouth will cure even eczema.

SYMPTOMATOLOGY

Pfaundler[27] states the case very clearly when he says that some children show a peculiar frequency in the disturbances of their health, no matter how carefully they are guarded against the causes which are known to produce these attacks. This proves to him conclusively that these children possess in their organisms some peculiarity in the form of a special disposition, an increased readiness towards certain disturbances, a diathesis. He differentiates the manifestations of exudative diathesis as primary, secondary and concomitant.

Skin.—This being the one organ which will naturally show the changes due to exudative diathesis most readily and at the same time most clearly, has therefore been studied very closely.

According to Feer[28] eczema is the expression of a chronic constitutional abnormality. There is no acute eczema, only acute exacerbations. Acute dermatitis is mistaken for eczema, as is proved by the

21. Steinitz, F., and Weigert, R.: Stoffwechselversuche am Säuglingen mit exsudativer Diathese, Monatsschr. f. Kinderh., 1910, lxxiv, 385.

22. Riesel, H.: Adipositas and exsudative Diathese, Ztschr. f. Kinderh., Orig., 1911, ii, 325.

23. Maillet, F.: Le tissu cellulaire sous-cutané dans la défense de l'organisme de l'enfant, reviewed in Ztschr. f. Kinderh., 1912, Referate, iii, 319.

24. Mendelsohn: Die Frage des Arthritismus, Med. Klin., 1911, vii, 752; Deutsch. Med. Wchnschr., 1911, xxxviii, 857.

25. Bouchard: Maladies par ralentissement de la nutrition, Paris, 1882.; Bouchard: Traité de pathologie générale, Paris, 1900, iii.

26. Pässler: Sind die sogenannten Diathesen Konstitutionsanomalien? reviewed in Jahrb. f. Kinderh., 1914, lxxix, 500.

27. v. Pflaundler, M.: Besondere Krankheitsbereitschaften (Diathesen) und Konstitutionsanomalien, Feer's Lehrbuch der Kinderheilkunde, 1914, Ed. 3, p. 183.

28. Feer, E.: Das Ekzem mit besonderer Berücksichtigung des Kindersalters, reviewed in Ztschr. f. Kinderh., 1913, Referate, iii, 66.

results of treatment. Eczematous conditions are not skin diseases *sui generis,* but merely the symptoms of a constitutional abnormality, often in connection with external stimuli. Scrofular eczema is not the sum of tuberculosis and eczema, but through the tuberculous infection of the organism the eczema acquires a changed character which gives it its specific appearance.

Bloch[29] sees in the diathesis a chemical allergy. To him the diathetic dermatosis is a reaction of the allergetic skin to accidental irritation, which latter may be endogenous or exogenous in origin.

Rachmilewitch[30] found that slight injury to the skin followed by irritation of the same (by mustard) caused a typical reaction, not only in children with manifest exudative diathesis, but also in the latent cases, and in the new-born.

Mautner,[31] on the other hand, finds no difference between healthy and eczematous children in their reaction to cataplasms or to bacterial irritation.

Hirschberg[32] puts stress on the importance of heredity, disposition, disturbances of digestion and metabolism for the development of eczema, especially in children.

Schlesinger[33] found the weight of infants with universal eczema, and still more of those with localized eczema, especially during the first three months of life, to be higher than in other diseases of infancy.

Schkarin[34] never missed other symptoms of a constitutional abnormality in connection with eczema, such as exudations into the skin and mucous membranes, which influence the course of nutrition.

Moro and Kolb[35] consider that the inclination to intertrigo in early infancy, to urticaria later, and to reactive inflammations at school-age are due to a lability in the vasomotors.

Lymphatic Apparatus.—Czerny[36] considers the affections in the lymphatic glands in exudative diathesis never to be primary, but always

29. Bloch, I.: Diathesen in der Dermatologie, reviewed in Deutsch. med. Wchnschr., 1911, xxxviii, 857.

30. Rachmilewitch: Hautreaktionen von Kindern mit exsudativer Diathese, Jahrb. f. Kinderh., 1913, lxxvii, 176.

31. Mautner, F.: Ueber Hautreaktion bei gesunden und ekzematösen Kindern, Ztschr. f. Kinderh., 1913, Orig., viii, 461.

32. Hirschberg, M.: Ekzem und innere Erkrankungen, reviewed in Ztschr. f. Kinderh., 1913, Referate, vii, 327.

33. Schlesinger, E.: Das Körpergewicht hautkranker, besonders ekzematöser Säuglinge, reviewed in Jahrb. f. Kinderh., 1908, lxvii, 467.

34. Schkarin, A.: Ueber Ekzema bei Säuglingen im Anschluss an die Lehre von Diathesen im Kindesalter, Jahrb. f. Kinderh., 1914, lxxviii, 156.

35. Moro, E., and Kolb, L.: Ueber das Shicksal von Ekzemkindern, Monatsschr. f. Kinderh., 1910, ix, 428.

36. Czerny, A.: Exsudative Diathese, Skrophulose und Tuberkulose, Jahrb. f. Kinderh., 1909, lx, 529.

to be secondary to pathologic processes in the skin and mucous membranes. The condition of the lymphoid organs, the thymus, spleen, tonsils, intestinal follicles, is independent of that of the lymph-glands. Their hypertrophy is due to overfeeding which favors the depositing of fat.

Benfey and Bahrdt[37] studied thirteen patients, none of whom had infantile eczema or tuberculosis; the clinical picture of these was dominated by adenoids and by regional glandular swellings.

Blood.—Kroll-Lifschütz[38] regards eosinophilia as a coordinated symptom of exudative diathesis.

Helmholz[39] and Rosenstern[40] both find eosinophilia accompanying eczema.

Putzig[41] has investigated a large material with the most careful methods and finds that healthy children have the same eosinophil count as have adults, whilst infants who later show signs of exudative diathesis have an increase in the eosinophils quite early. He concludes that eosinophilia is a symptom of exudative diathesis.

Aschenheim,[42] on the other hand, considers eosinophilia as a special disposition or diathesis, which is not identical with exudative diathesis but frequently combined with it.

Respiratory Apparatus.—Czerny[13] sees a great similarity in the affections of the air-passages to those of the skin. His views differ greatly from those of the French school, who consider asthma and bronchitis to be due to arthritism or herpetism, as, for instance, Goilav,[43] Merkel[44] and Spolverini.[45] Some children suffer from repeated affections of the same parts of the respiratory mucous membrane and in the same manner. One child has pharyngitis several times a year, another follicular angina, a third an infection of the

37. Benfey, A., and Bahrdt, H.: Beitrag zur Beurteilung der Drüsenschwellungen bei Kindern jenseits des Säuglingsalters und ihrer Beziehungen zum Lymphatismus, Ztschr. f. Kinderh., 1913, Orig., vii, 481.

38. Kroll-Lifschütz, A.: Zur Frage der Eosinophilie und exsudativen Diathese, reviewed in Ztschr. f. Kinderh., 1914, Referate, viii, 291.

39. Helmholz, H.: Eosinophile Blutkörperchen bei akutem exsudativem Ekzem, Jahrb. f. Kinderh., 1908, lxix.

40. Rosenstern, J.: Exsudative Diathese und Eosinophilie, Jahrb. f. Kinderh., 1908, lxix, 631.

41. Putzig, H.: Das Vorkommen und die klinische Bedeutung der eosinophilen Zellen im Säuglingsalter, besondere bei exsudativer Diathese, Ztschr. f. Kinderh., 1913, Orig., ix, 429.

42. Aschenheim, E.: Eosinophilie und exudative Diathese, Jahrb. f. Kinderh., 1912, lxxvi, 456; Ist die Eosinophilie ein Symptom dêr exsudativen Diathese? Ztschr. f. Kinderh., Orig., 1914, x, 503.

43. Goilav: Etude sur la bronchite liée a l'herpétisme, Thèse de Paris, 1889.

44. Merkel: L'asthme chez les enfants, Thèze de Paris, 1901.

45. Spolverini, I. M.: Sulla etiologia e terapia dell'asthma essenziale nei bambini, reviewed in Ztschr. f. Kinderh., 1914, Referate, vii, 221.

pharyngeal tonsil, a fourth pseudocroup, a fifth bronchitis diffusa. The different attacks are very similar, and we must therefore assume that the same local disposition exists as in seborrhea, the difference consisting only in the form of the reaction to equivalent pathologic irritation.

Digestive Apparatus.—Lingua geographica is according to Groos[46] most likely constitutional, and is found in the hereditary neuropathic type of individuals.

Lublinski[47] denies its connection with exudative diathesis.

Klausner[48] considers it congenital and consequent irritability of the mucosa of the tongue, and he states that dermatologists do not agree that it is part of the exudative diathesis.

Czerny[13] however regards it as one of the first symptoms of exudative diathesis, which may at times be seen during the first month of life, but only in the living child.

The appendix was examined by Lieblein,[49] who found considerable hyperplasia of its lymphatic apparatus and very long appendices in six young people with pronounced lymphatism.

Langstein[50] could not find any pathogenic organisms in many cases of infants in whose stools he had noticed pus. These infants had the clinical manifestations of exudative diathesis, and he believes that in this a special disposition to intestinal symptoms exists, which will result in mucus in the stools in light cases, and pus in the severe ones. He sees in the hyperplasia of the intestinal follicles, which was first described by Czerny,[51] the reason why infants with exudative diathesis react to noxae which do not affect healthy infants.

Genito-Urinary Apparatus.—Lust[52] found in the sediment of apparently normal urine which he had centrifuged, epithelium and a few leukocytes as a sign of a process of desquamation in the urogenital mucosa in more than 50 per cent. of the children with exudative diathesis.

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46. Groos, F.: Die Landkartenzunge, reviewed in Ztschr. f. Kinderh., 1913, Referate, vii, 54.

47. Lublinski, W.: Ist die Landkartenzunge erblich? Deutsch. Med. Wchnschr., 1910, xxxvi, 2343.

48. Klausner, E.: Ueber lingua geographica hereditaria, reviewed in Jahrb. f. Kinderk., 1911, lxxiv, 120.

49. Lieblein, V.: Zur Kenntniss der lymphatischen Pseudoappendicitis, reviewed in Ztschr. f. Kinderh., 1912, Referate, iii, 637.

50. Langstein, L.: Erscheinungen von seiten des Magendarmkanals bei exsudativer Diathese, reviewed in Jahrb. f. Kinderh., 1908, lxvii, 613.

51. Czerny, A.: Zur Kenntniss der exsudativen Diathese, Jahrb. f. Kinderh., 1908, lxviii, 513.

52. Lust, F.: Die Beteiligung der Schleimhaut des Urogenitalapparates am Symptomenkomplex der exsudativen Diathese, reviewed in Jahrb. f. Kinderh., 1912, lxxvi, 99.

Beck[53] in his study of forty cases of his own confirms Lust's findings of desquamative processes on the mucosa of the efferent urinary passages.

Nervous System.—Saenger[54] considers the psychic element very important as supplementing the somatic disposition of exudative diathesis.

Czerny[55] lays stress on the close connections between the neuropsychopathies and exudative diathesis, though he does not look on this as causative but only as a combination. Frequently the education of the child has been faulty owing to the exudative diathesis, and thus the neuropsychopathies have been favored. This explains the remarkable results which have often been observed under psychic treatment in children with intractable eczema or asthma, sometimes also in processes originating in the nasopharynx.

Pfaundler[56] calls the attention of physicians to cases seen frequently in which the symptoms of the lymphatic constitution are combined with those of neuropathy to form what he calls neurolymphatism. In these cases the nervous manifestations, the severity of the reflexes, are of special importance; as, for instance, the spasmodic sneezing in coryza, the pseudocroup in laryngitis, the pertussoid in bronchitis, the asthma in bronchiolitis, severe colic and mucomembranous diarrhea in enteritis, enuresis in balanitis, blepharospasm in conjunctivitis.

Czerny[13] explains clearly that the severity of the itching is dependent on the degree of irritability of the nervous system. The itching causes the children to scratch, and then the danger of a secondary infection and thus of an eczema is great. He warns physicians not to neglect the child's psyche over its body.

The Eyes.—Igersheimer[57] found in 70 per cent. of 152 children with phlycten a positive v. Pirquet reaction. He urges in these cases the treatment of the exudative diathesis, and he advises great care in keeping these children away from people suffering from tuberculosis.

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53. Beck, C.: Die Beteiligung der Schleimhäute des Urogenitalapparates am Symptomenkomplex der exsudativen Diathese, reviewed in Jahrb. f. Kinderh., 1914, lxxviii, 495.

54. Saenger, M.: Ueber die psychische Komponente unter den Asthmaursachen, reviewed in Ztschr. f. Kinderh., 1912, Referate, iii, 244.

55. Czerny, A.: Zur Kenntniss der exsudativen Diathese, reviewed in Jahrb. f. Kinderh., 1908, lxviii, 634.

56. Pflaundler, M.: Ueber kombinierte Krankheitsbereitschaften oder Diathesen im Kindesalter, reviewed in Jahrb. f. Kinderh., 1911, lxxiv, 601.

57. Igersheimer: Ueber die Beziehungen von Skrophulose, Lymphatismus, exsudativer Diathese zu den Erkrankungen des Auges, reviewed in Jahrb. f. Kinderh., 1911, lxxiii, 271.

METABOLISM

Menschikoff[58] has investigated the metabolism of children with exudative diathesis and finds that they react easier to differences in the ingestion of chlorin, increases as well as decreases, and more so with manifest than with latent symptoms.

Bernis[59] and Kern[60] look on the change in the nitrogen metabolism as characteristic. The latter found that children with exudative diathesis have a delayed excretion of uric acid.

Czerny[36] is convinced that the metabolism of fat is disturbed. Finkelstein and Meyer claim to have found the reason for the changes in the altered metabolism of the salts.

CONNECTION WITH OTHER DISEASES

v. Hansemann[61] states that many diseases develop on the basis of either acquired or congenital constitutional abnormalities, which consist in anatomic or metabolic changes. The composition of the body fluids and the activity of the cells form the medium through which the growth of the pathologic elements may be either favored or destroyed. Some causes, like colds, or general diseases, like gout or rickets, also age and inheritance, will cause a change in the composition of the body fluids.

Unterberger[62] sees in the constitution a factor which is of paramount importance, especially in the development of tuberculosis, against which the action of the bacteria may be neglected.

Rozenblat[63] is doubtful about the connection between scrofulosis and exudative diathesis.

Czerny[64] clearly defines his standpoint when he writes:

> The identical infectious agent does not produce similar clinical pictures in different individuals. This is due only partially to the quantity or quality of the micro-organism or its location in the body. The appearance of certain symptoms of infectious diseases and their course depends mainly on individual constitutional abnormalities. These may be either congenital or acquired; they may affect either single organs or the whole body.

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58. Menschikoff, V.: Chlorretention bei exsudativen Prozessen der Haut, reviewed in Jahrb. f. Kinderh., 1912, lxxvi, 99.

59. Bernis, A. L.: Répartition de l'azote urinaire dans quelques dermatoses dites diathésiques, Dissertation, Bordeaux, 1912.

60. Kern, H.: Ueber Harnsäureausscheidung bei exsudativen Kindern und ihre Beeinflussung durch Atophan, Jahrb. f. Kinderh., 1913, lxxviii, 141.

61. v. Hansemann: Die Konstitution als Grundlage von Krankheiten, Med. Klin., 1912, viii, 933.

62. Unterberger, S.: Die Bedeutung der Konstitution für den Verlauf der Krankheiten, reviewed in Ztschr. f. Kinderh., 1912, Referate, iii, 411.

63. Rozenblat, H.: Scrophulosis, lymphatismus, diathesis exsudativa, reviewed in Jahrb. f. Kinderh., 1910, lxxii, 648.

64. Czerny, A.: Die Bedeutung der Konstitution für die Klinik der kindlichen Infektionskrankheiten, reviewed in Ztschr. f. Kinderh., 1914, vii, 354.

Engel[65] is of the opinion that scrofulosis develops on the soil of exudative diathesis, the infection with the tubercle bacillus being added to the constitutional abnormality.

THERAPY

Feeding.—Czerny[36] sums up his views on the connection between exudative diathesis and feeding as follows: The idea that milk and eggs are the best food for children is erroneous, and it is most likely a relic of the days when rickets and scrofulosis were regarded as diseases due to an insufficient supply of protein in the food. The general statement that woman's milk is the best food for infants is also wrong. We can only assert that the mortality amongst children at the breast is lowest. Many children do not thrive at the breast and show all kinds of symptoms while on this food. These disturbances are due to constitutional abnormalities, of which exudative diathesis is one. Thus, for instance, seborrhea faciei is due to the feeding which brings out the exudative diathesis, and one of the symptoms of this is seborrhea. The first two years of life are of the greatest importance as concerns the appearance of exudative diathesis.

Czerny[13] further states that three points are of importance in the control of exudative diathesis, namely: (1) the kind of feeding; (2) the condition of the nervous system; (3) intercurrent infections. By treating this trio we can reduce the symptoms of exudative diathesis to a minimum.

Feer[66] believes that the congenital disposition and the mode of feeding should be considered as the causes of exudative diathesis. To fight the disposition these children must be fed sparsely; they must not get milk, butter, eggs or meat; they should have little sugar; they are allowed large amounts of fruit and vegetables.

Simpson,[67] on the other hand, denies the harmful effect of milk in infants with eczema, and he does not want to change the diet of the infant as long as it is thriving.

Finkelstein[68] is of the opinion that the relation between eczema and the mode of feeding and the gain in weight are by no means simple.

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65. Engel: Die Skrophulose und ihre Behandlung, Med. Klin., 1913, ix, 2099.
66. Feer, E.: Ueber exsudative Diathese des Kindes, reviewed in Ztschr. f. Kinderh., 1912, Referate, i, 679.
67. Simpson, C. A.: Infantile eczema, Jour. Am. Med. Assn., 1912, lviii, 995.
68. Finkelstein, H.: Zur diätetischen Behandlung des Säuglings- und Kinderekzems, Ztschr. f. Kinderh., 1913, viii, Orig., 1.

Steinitz[69] in his report from the Vegetarian Children's Home in Breslau, attributes to the diet his good results in keeping down the manifestations of exudative diathesis.

Variot[70] asserts that eczema is due to the "eczematigenous" qualities of mother's milk and that it may be cured by a change in the wet-nurse or in the food. Ibrahim, who reviews this paper, asks, however, why this milk was not tried on other babies who did not have exudative diathesis.

Czerny[71] cites a very interesting experiment which proved to him that the clinical picture, which was formerly called scrofulosis, is a combination of the symptoms of tuberculosis and of exudative diathesis.

Climate.—Von Planta[72] believes that the lessened amount of oxygen in the mountain air causes a change in the metabolism, and he therefore advises a long-continued sojourn of not less than one year.

Bockhorn[73] advises a sojourn of three months at the seashore for children with exudative diathesis.

Drugs.—Krasnogorski[74] proclaims himself an adherent of the theory of Eppinger and Hess, who attribute some of the symptoms of exudative diathesis to vagotomy, and he therefore recommends the administration of atropin in increasing doses.

Schreiber[75] has seen good results from the alkaline mineral waters, also arsenic periodically, and calcium glycerophosphate.

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69. Steinitz: Ueber Vegetarismus und exsudative Diathese, Jahrb. f. Kinderh., 1907, lxv, 513.

70. Variot, G.: Beobachtungen über die Behandlung des Säuglingsekzems durch Milchwechsel, reviewed in Jahrb. f. Kinderh., 1912, lxxv, 390.

71 Czerny, A.: Beitrag zur Leberthrantherapie, reviewed in Ztschr. f. Kinderh., 1913, Referate, iii, 338.

72. v. Planta: Die exsudative Diathese und das hochalpine Gebirgsklima, reviewed in Ztschr. f. Kinderh., 1912, Referate, i, 600.

73. Bockhorn, M.: Die exsudativ-lymphatische Diathese und die Prophylaxe, Deutsch. med. Wchnschr., 1914, xl, 960.

74. Krasnogorski, N.: Exsudative Diathese, Vagotonie, reviewed in Jahrb. f. Kinderh., 1914, lxxviii, 495.

75. Schreiber, G.: Les Diathèses infantiles, Arch. de méd. d. enf., 1912, xv, 433.

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